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## **BACK TO SACAJAWEA\***

#### Presidential Address

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T IS a particular source of satisfaction to me that my tenure of office should I coincide with the historic Silver Anniversary of the founding of the Central Association here in St. Louis. This city which saw the birth of our Society is noteworthy for many scientific and cultural achievements. We commemorated one of the major scientific events of the century during this meeting when we honored Dr. Edward A. Doisy on the twenty-fifth anniversary of his discovery of crystalline estrogen. I need not dwell at length upon other lasting contributions to our specialty by St. Louis members of the profession. The names of Crossen, Ehrenfest, Engelmann, Gehrung, Gellhorn, Schwarz, Taussig, and others have been indelibly etched upon medical annals. I cannot refrain from mentioning also that the investigations which have elevated our fellow member, Dr. William Dieckmann, to the position of a world authority on the toxemias of pregnancy had their beginnings when he was active in St. Louis. Dr. Willard Allen, a member of our Society, whose fundamental researches established our present knowledge of progesterone, now resides in St. Louis. A spirit of individual initiative and earnest devotion to the advancement of knowledge long has dominated this medical community.

When we speak, then, of the "Spirit of St. Louis," we think not only of Lindbergh and his famous flight, but also of other adventures which had their

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beginnings in this metropolis on the Mississippi. It was here that a pioneer venture in education, the first public kindergarten, was undertaken eighty years ago. Long before, however, this city was the starting point of more daring and hazardous exploits. Among many such we may recall those of Zebulon Pike and Pike's Peak and, most famous of all, the expedition headed by Meriwether Lewis and William Clark, who were charged by Thomas Jefferson to search the vast new territory acquired by the Louisiana Purchase and to find a water route to the Pacific Ocean.

It seems altogether appropriate at this time to commemorate the departure of Lewis and Clark from St. Louis, since exactly one hundred and fifty years ago they here began their epic of discovery, the scientific merits of which have never been duly appreciated in history books. Returning two years later, mission accomplished, they<sup>1, 2</sup> revealed to the world in their Journals accounts of unsurpassed heroism, sheer romanticism, and, more important, many contributions to knowledge in many fields of science. The records make interesting reading, even today, for geographers, geologists, ethnologists, linguists, biologists, and physicians—in short, for "all sorts and conditions of men." In the daily logbooks may be found intriguing details about such things as the spacing of a fish's eyes and the contents of its stomach; about the characteristics of the land, its flora and fauna, and the languages and diseases of its inhabitants. Psychologists even in 1954 will revel in the lurid portrayals of human behavior which rival the revelations of both volumes of the Kinsey Report. (It may have been sheer coincidence that a Mr. McKinsey was, in fact, a member of the expedition.) Even the ladies of this audience would be intrigued to read the fashion notes giving intimate details of petticoats, bras, and girdles, and of the doings of women in aboriginal society.

These and many other facts and opinions were reported to Thomas Jefferson and the American Philosophical Society. Today, here in the Jefferson Hotel and before this, I trust, equally philosophical gathering, I wish to reveal impressions gleaned from reading between the lines of the Lewis and Clark Journals about "natural childbirth," "early ambulation," and "demand feeding"—with some sidelights on the doctrine of "permissiveness" in child psychology and so-called "progressive education." The title of this literary pursuit is "Back to Sacajawea."

Sacajawea was a young Indian squaw, one of the wives of the French-Canadian interpreter and wife-beater, Toussaint Charbonneau, "a man of no particular merit." His child-bride, Sacajawea, on the other hand, was by all odds one of the most valuable and intrepid members of the party. She not only was highly intelligent but also must have been a woman of unusual vigor to have survived all of the hardships of the round trip alone, not to mention the coincident ordeals of pregnancy, labor, and puerperium and, later, if that were not enough, a possible attack of acute pelvic inflammatory disease as well.\*

<sup>\*</sup>Lewis wrote, Sunday, June 16, 1805: "I believe her disorder originated principally from an obstruction of the mensis in consequence of taking could."

The story begins quite naturally, and appropriately enough, nine months after the expedition left St. Louis, when Sacajawea had a baby. This obstetric event was recorded by Lewis, Feb. 11, 1805:

... about five oClock this evening one of the wives of Charbono was delivered of a fine boy. It is worthy of remark that this was the first child which this woman had boarn, and as is common in such cases her labour was tedious and the pain violent; Mr. Jessome informed me that he had frequently administered a small portion of the rattle of the rattle-snake, which he assured me had never failed to produce the desired effect, that of hastening the birth of the child; having the rattle of a snake by me I gave it to him and he administered two rings of it to the woman broken in small pieces with the fingers and added to a small quantity of water. Whether this medicine was truly the cause or not I shall not undertake to determine, but I was informed that she had not taken it more than ten minutes before she brought forth. perhaps this remedy may be worthy of future experiments, but I confess that I want faith as to its efficacy.

Much that could be gleaned from this simple case report I will not take the time to elaborate. Editors like Drs. Dieckmann, Eastman, and Reis might editorialize, even perhaps at great lengths, to point out that it is a model of conciseness and clarity. They would surely commend Lewis wholeheartedly for his scientific restraint and his insistence upon clinical experiments before drawing conclusions. Most certainly they would add a paragraph or two applauding his careful avoidance of the common error of post hoc ergo propter hoc and the still prevalent fallacy that one apparently beneficial swallow makes a panacea. From their published accounts of ruptured uteri, asphyxiated infants, and its disturbing effects upon the coronary circulation, it seems clear that "I.V.Pit," the modern oxytocic equivalent of the rattlesnake remedy for prolonged labor, still "biteth like a serpent and stingeth like an adder." We must agree with Lewis that there is need for "future experiments" since evidently all still is not well in this field of applied pharmacology.

But it is not of future experiments that I wish to speak today—rather, it is of present-day trials of Natural Childbirth which Lewis and Clark also included in their investigations as they journeyed from St. Louis toward the Pacific a century and a half ago. Why, they pondered, did many Indian women accomplish childbirth with singular "facility and ease," whereas other children of nature, like Sacajawea, had labors which were "tedious" and pains that were "violent"? Was parturition influenced by environmental conditions, such as climate and altitude? Could labor be made less difficult by exercise or was easy delivery simply a "gift of nature"? You can recognize many of the same questions being raised today.

After two years of studying the problem as they observed many different Indian tribes along the way, certain facts became evident. Lewis and Clark observed that easy labors were the rule among pure-bred Indians in all climates and regardless of whether the women exercised throughout the entire course of pregnancy by carrying "heavy burthens," or whether, indolently,

they indulged in the relative comforts of riding horseback.\* Ergo, they reasoned, ease of parturition (Natural Childbirth, if you will) is not a consequence of climate, altitude, or physical activity.

To such bits of negative evidence they next added some apparently positive information about dystocia when they learned from those "who were conversant with the fact" that "the indian women who are pregnant by whitemen experience more difficulty in childbirth than when pregnant by an Indian." Obstetric texts, it seems, have been remiss in not giving Lewis and Clark credit for recognizing long ago the genetic basis for what we now call cephalopelvic disproportion. What an obstetric Utopia we might now enjoy had they launched a successful propaganda for racial purity to eliminate half-breeds and to give us truly natural childbirth without fear—of dystocia, that is! Many years later, George Engelmann,3† the learned St. Louis obstetrician, after identical observations among the Indians, also suggested that dystocia, so prevalent among civilized women, might be a consequence of intermarriage between people of different races and skeletal types. His hints that eugenics might provide the answer for easy childbearing also went unheeded. And so, love still remains triumphant and, in the American melting pot, continues to beget disproportion.

Cautious scientists that they were, Lewis and Clark drew no hasty conclusions and evolved no plans for Utopian childbearing. From their childhood lessons they remembered, no doubt, that Mother Eve, a thoroughbred primitive if there ever was one, also brought forth "in sorrow." Moreover, observing the ways of their men and the Indian maids they wisely decided to let the matter drop and made no further notes on the subject. The solution, they must have surmised, was not as simple as it had seemed at first blush.

Nor is the solution offered by the Natural Childbirth enthusiasts of our times—I mean particularly the glib writers of our lay journals—as easy as all that. From their writings Eve's daughters and the Sacajaweas of today have inferred that setting-up exercises, plus lectures on the facts of life, speak a

"We see then certain differences and an increase of the difficulties of labor as civilization is neared. How different are the conditions upon which I have laid stress as existing, among savage tribes, from those we find in our centres of luxury! People intermarry regardless of race or frame of body and the consequence is the frequent disproportion between the head of the child and the pelvis of the mother."

<sup>\*&</sup>quot;... one of the women who had been assisting in the transportation of the baggage halted at a little run about a mile behind us, and sent on the two pack horses which she had been conducting by one of her female friends. I enquired of Cameahwait the cause of her detention, and was informed by him in an unconcerned manner that she had halted to bring fourth a child and would soon overtake us; in about an hour the woman arrived with her newborn babe and passed us on her way to the camp apparently as well as she ever was. It appears to me the facility and ease with which the women of the aborigines of North America bring fourth their children is rather a gift of nature than depending as some have supposed on the habitude of carrying heavy burthens on their backs while in a state of pregnancy, if a pure and dry air, an elivated and cold country is unfavourable to childbirth, we might expect every difficult incident to that operation of nature in this part of the continent; again as the snake Indians possess an abundance of horses, their women are seldom compelled like those in other parts of the continent to carry burthens on their backs, yet they have their children with equal convenience, and it is a rare occurrence for any of them to experience difficulty in childbirth. I have been several times informed by those who were conversant with the fact, that the indian women who are pregnant by whitemen experience more difficulty in childbirth than when pregnant by an Indian. If this be true it would go far in support of the opinion I have advanced . . ." Lewis, Monday, Aug. 26, 1805.

†"Positive statements from several of the Indian tribes indisputably prove the truth of this rule; thus many of the Umpqua squaws die in childbed with half-breed children, whose large-sized heads do not permit their exit. The Umpqua mother will be easily delivered of an offspring from an Umpqua father, but the head and body of a half-breed child is apt to be too large to pass through her pelvis. . . "We see then certain differences and

magic open sesame to the parturient canal. As a result of oversimplified and distorted accounts, many of your patients and mine have been deluded into thinking that ritualistic contortions and scientific incantations are the factors which make delivery drugless, painless, expeditious, and entirely safe. What is more, they have been led to believe, if only by innuendo, that all the modern advances in analgesia, anesthesia, and other ancillary procedures are not only superfluous but physically and emotionally detrimental to themselves and their offspring!

Mind you, I am speaking only of the overenthusiastic zealots who deny or minimize the physical discomforts of parturition, disregarding the fact that in practically every language uterine contractions of labor are called "pains." Such unrealistic teachings can only bring about a large harvest of disillusionments and, eventually, for those who fail, a revival of the old dreads of ordeal and suffering which mothers of the past few decades have been spared. Today's fearless young primigravida has not been brought up on accounts of the horrors of labor with which grandma regaled her children. Consequently, Mrs. Sacajawea of today usually approaches the prospect of labor without overwhelming fear. If she then succeeds in carrying out a program of completely drugless labor the achievement may be partially credited to the fact that she had been suitably conditioned by matter-of-fact accounts of her own birth, mercifully eased, let us hope, by a judicious amount of analgesia. If she fails, for one reason or another, and if her obstetrician is one of the all-out enthusiasts who persist to the point of denying the benefits of any drug for the relief of pain "we shall be back," says Eastman, "to the 'wailing rooms' of old and the vicious circle will be complete."

I heard one such disillusioned gravida reacting from general anesthesia after an unsuccessful trial of Natural Childbirth: "Dr. Read," she shouted for all to hear, "is for the birds!" Something was amiss. Quite obviously she had failed to achieve the easy labor she had expected simply from reading his book and from performing relaxation exercises, unaware that relaxation reflects an attitude of mind and a feeling of confidence and calm. Like others she had expected these superficial rituals to set up conditioned reflexes automatically eliminating physical discomforts, the pains of fear and the fears of pain—all in ten easy lessons. Now, thoroughly disillusioned with her medical attendant and with herself, it will be hard for her to accept, even as she lies comfortably on the psychiatrist's couch, that the processes of parturition on the delivery table are pleasant, painless, and exhibitanting experiences—and that her mental well-being and her relationships to her baby were shattered because she did not consciously participate in the act of expulsion. Others, more suggestible, may carry away as aftermaths enduring feelings of guilt and inferiority because of failure and of their weakness in accepting painrelieving agents. A willy-nilly, all-out program is bound to fail often. Even Lewis and Clark, neither one a physician, knew that in primiparas "as is usual" the pains are "violent" and the labors "tedious."

Oh, come now, I can hear the writers say. You know what we mean. Certainly, we know what they should mean, namely, that there is a middle

road, but unfortunately their lay readers don't—no more than readers did in the days when lay writers played others tunes of "painless childbirth" and "twilight sleep," ad lib. and unlimited. Quite recently, Edith M. Stern, who describes herself as a "veteran writer of medical and psychological articles for the mass-circulation 'slicks,'" penitently confessed past sins in the "torrent of popularization" in an article called "Medical Journalism—With and Without Upbeat." In this confession of guilt she adds the hope of reform:

"Busily my writing colleagues and I are beginning—for good money, to be sure, but also in good faith—to correct some of the impressions we have created, also in good faith and for good money. Today the keynote in articles about antibiotics is no longer "Eureka" but "Caution." Recently a woman's magazine article mentioned "disproportionate dread of polio." Into psychiatric articles an organic note is creeping as, similarly, the adjuration that there are times to say 'don't' to a child slipping into the kind of piece which, formerly, would have gone all-out for 'permissiveness.'"

These lines and other suggestions by Edith Stern also carry an implicit warning to members of our own profession who prematurely publish their trials but seldom acknowledge subsequent failures and shortcomings. Long ago and many times since the address of our second President, Dr. Fred J. Taussig, in 1932, on "Safer Motherhood Versus Easier Motherhood," other members of this Society have warned of the risks of various forms of radicalism in obstetrics which inspire snappily written but uncritical popularizations. It is welcome news that an about-face in journalism may be in the making, let us hope before the salutary objectives of childbirth without fear are hopelessly sold down the river.

As Lewis and Clark journeyed up the Missouri River in what is now South Dakota they saw the mouth of the Grand River "throwing out mud with Small propotion of Sand." On its banks, however, they noted that "great quantities of red Berries, ressembling Currents, are on the river in every bend." So, too, we may regard the torrent of talk about Natural Childbirth, for, beyond the froth and mud of exaggerated claims and misinterpretations lie the red berries of a fruitful field of better human relations.

In the world of commerce and industry, cultivation of this field through educational media has long replaced the "public be damned" attitude of the old tycoons. Call it public relations, labor relations, or just plain advertising, successful corporations know that without concern for public regard their chances for economic health and survival nowadays are nil. Within recent time we have heard repeatedly that our own profession—our schools, hospitals, and our practitioners of medicine at all levels—should take a tip from the corporations, both in the interest of retaining public esteem and in the interest of achieving better and more effective medical care.

In their efforts to interject educational methods into maternity care, the proponents of so-called physiological childbirth may have found a way of helping to do just that. Beyond the high-pitched emotionalism which permeates much of the talk, the ultimate benefits of natural childbirth techniques

may be more along the line of restoring some of the former confidence with which patients regarded their physicians. And from such better relationships between physicians and patients better healing also may come.

Let us make no mistake about it: A recent rash of articles in the lay press has been highly and often justly critical of many phases of medical care. One of the most sympathetic and searching of these states in its title, "The M.D.'s Are Off Their Pedestal" and sums up our fall from public grace by saying simply: "It isn't because some doctors are accused of being fastmoney men. It's because most doctors practice a new and better brand of medicine that leaves many people cold while it makes them well." This is another way of saying that people respect our shots of penicillin, our wonderful anesthetics, and our omniscient x-rays, and all the many other fancy tests and gadgets we employ but that we have lost the human touch. The author of this article, Herrymon Maurer, goes on to point out that physicians must learn "that humanity is an inseparable part of science. Their patients like them best when they avoid impersonality, which is one of the most persistent complaints about medical care."

Such complaints come in an age when we as physicians presume to recognize the patient as a person who is afflicted, not only with the organic but also with the psychological components of disease. Small wonder, therefore, that it is the geriatric patient who seems most often to speak wistfully of the good, usually old, doctor long departed to his rewards, "who pulled me through." You and I know, of course, that most often he probably did no such thing. His stock of specific, effective remedies and manual skills was pitifully small but his stock of humanity was large, greater by far than his scientific knowledge. But patients loved him because he appeared as a tower of strength and wisdom to bolster their morale while, as Paré admitted in all honesty, "God cured him."

Much of the success of Lewis and Clark in exploring the wilderness can be laid to their mastery of primitive psychology and their ability to foster good human relations. When supplies of trinkets and food were exhausted they gained the good will of the natives by practicing medicine. They achieved some apparently remarkable cures and, what is more important, gained the help and confidence of the savages.\*

Even today it is obvious that, by and large, successful physicians quite uniformly display greater human warmth, often lightly called "bedside man-

<sup>\*</sup>Monday, May 5, 1806, Clark wrote: "... at the second Lodge of Eight families Capt L. & myself both entered smoked with a man who appeared to be a principal man. as we were about to leave his lodge and proceed on our journey, he brought forward a very eligant Gray mare and gave her to me, requesting some eye water. I gave him a phial of Eye water a handkerchief and some small articles of which he appeared much pleased. while we were encamped last fall at the entrance of Chopunnish river, I gave an Indian man some Volitile liniment to rub his knee and thye for a pain of which he complained, the fellow soon after recovered and have never seased to extol the virtue of our medicines, near the enterance of the Kooskooske, as we decended last fall I met with a man, who could not walk with a tumure on his thye, this had been very bad and recovering fast. I gave this man a jentle pirge cleaned and dressed his sore and left him some casteel soap to wash the sore which soon got well. this man also assigned the restoration of his leg to me, those two cures has raised my reputation and given those native an exoited oppinion of my skill as a phi(si)cian. I have already received many applications, in our present situation I think it pardonable to continue this deception for they will not give us an provisions without compensation in merchandize, and our stock is now reduced to a mear handful. We take care to give them no article which can possibly injure them, and in maney cases can administer & give such medicine, & sirgical aid as will effectually restore in simple cases &c."

ner," than many of their possibly scientifically better-informed but indifferent colleagues. Call it what you will, the attending physician, in the true sense of the word, adheres to the precise dictionary definition of attend, namely, "to direct the mind or observant faculties, to listen, apply oneself; to watch over, minister, wait upon, follow, frequent." In his classic treatise, "The Care of the Patient," the late Dr. Francis Peabody summarized all this even more succinctly: "One of the essential qualities of the clinician is interest in humanity, for the secret of the care of the patient is caring for the patient."

We as obstetricians and gynecologists caring for problems involving the reproductive functions are confronted with the need for understanding human emotions more frequently perhaps than are other specialists in medicine. Certainly for us they often lie more close to the surface, though many times effectively masked by feminine wiles. None the less, in our very busyness with techniques and skills we fail often, as the saying goes, "to see the woods for the trees." "The greatest weakness in American obstetrics," says Eastman, 8 "is lack of emotional support in pregnancy and labor." Critical self-analysis, I think, will convince us that this is true and that in our maternity care we are long on such things as nutritional, metabolic, and cardiovascular support, but too often we are woefully short in our dealings with the little worries and queries which loom so large in the minds of our patients. You know all the superstitions and taboos, the doubts and the anxieties that plague them little things but their own-which should be belayed and allayed before they end up in such manifestations of fear as "psychogenic dystocia." Eastman's beautifully written summary in the section on "Psychological Approach to the Patient" should be prominently posted in every maternity unit so that all who read may heed.

The gist of the matter, as I see it from those who practice Natural Childbirth realistically, is that it consists of an effort to assist the patient intellectually in minimizing the anxieties which would come from ignorance, lack of understanding, and loss of confidence. No matter how conscientious, the average obstetrician simply does not have the time and energy necessary to do this job thoroughly for each individual during a busy office routine. Supplementation of antenatal care with classes, skillfully supervised lest they arouse rather than allay anxieties, should help to fill these needs. The best locale for such a program is at the hospital in which confinement is to occur, where the expectant mother has a chance to glimpse, even if only at a long range, the facilities available for her care during labor and post partum and for the care of her infant. Equally important is the opportunity to meet and see some of the people who will help her doctor to see her through the coming event. She and her husband should know that there are adequate facilities, equipment, supplies, and personnel which will be directed toward her safety and comfort and that of her child. The most important effect of such programs is the creation in the patients of the feeling that they are going to enter familiar, sympathetic surroundings and be amid people who are genuinely interested in their welfare. It is gratifying that an increasing number of hospitals have seen the advantages to be derived from such techniques and the opportunity

to prove that humanity can coexist with the science of modern obstetrics. Robert N. Creadick<sup>10</sup> has recently published an outline for his program of prenatal support during pregnancy and labor designed to build sound physician-patient-hospital relationships. It ends with the significant note: "No patient is to be denied analgesia or sedation during labor if such is desired."

It is entirely unreasonable, of course, to suppose that prenatal classes, with or without calisthenics to induce relaxation, will greatly improve human relations without teamwork all along the line—from the obstetrician's office to the hospital and back again. This teamwork demands the cooperation of our office receptionists and technicians and in the hospital of the admitting clerks, the nursing personnel, the house staff—and the attending physician himself—all of whom are more efficient and better educated than ever before. Such efficiency, however, must be made of kinder, not sterner, stuff.

It will take little short of a revolution to bring about this Utopia of brotherhood and light, especially in these days of understaffed maternity units where the milk of human kindness often is in short supply and where such simple acts as wiping a sweat-covered brow, moistening parched lips, or offering a reassuring smile too often seem hard to come by. Much as we may take pride in the superior educational standards of the modern nurse, such simple bedside services appear to have been de-emphasized in our superscientific curricula. In an editorial note on a paper by Elizabeth Tylden, "Psychology and the Maternity Unit," Eastman<sup>11</sup> made these comments:

To cite one of our failings, it is a sad commentary on the hospital management of parturients that patients in active labor are often left alone—sometimes while a handful of nurses at a nearby office are busy with charts or other routine minutiae. Indeed, if a nurse today ventures to sit with a normal parturient at the expense of neglecting her paper work, she is certain to catch hell from the higher ups. There is something wrong here and, as is true of so many other issues of our day, something should be done about it.

To this all will add fervent and loud amens, with an encore for his next line supporting Tylden's views on better psychological methods of handling patients: "Precepts such as these," says Eastman, "are vastly more important than knowing the pH of the pigeon's egg or how to make an accurate inventory of the linen closet."

It is gratifying to see that already some sort of a minor revolution or reformation is under way and that some educators in nursing are seeing the errors and are returning student nurses from the laboratories to the bedside earlier than in recent years. It is to be hoped that other courageous heads of nursing will do likewise and dethrone the armchair theorists of nursing by remote control. Medical schools have long since broken away from purely didactic teaching and very early in his training have placed the student in the wards to see the human being himself and learn to know more than the text-book version of the patient. Also noteworthy is the fact that many educators are urging introduction of more of the humanities in undergraduate preparation for medicine.

From still another angle, but also pursuing the goal of providing better patient care through improved human relations, hospital administrators have also seen the light. A noteworthy contribution along this line, I am pleased to say, was made from my own hospital. In her recently published book, "The Improvement of Patient Care. A Study at Harper Hospital," the Associate Director, Marion Wright, 12 had this to say: "It is well understood that a patient's mental state during much of the hospital stay has a very definite reaction upon his physical condition. . . . Throughout it was recognized that little could be done without positive good will, the active participation and the considered judgments, of all those within our own organizations who contribute directly or indirectly to the object of all hospital concern—the patient." Miss Wright's study, primarily based upon critical self-analysis, points out many ways and means of improving patient care—even in these days of personnel shortage, the 40-hour week and the trade-union attitude toward work which has infiltrated even some professional circles.

In all fairness we, as obstetricians, must admit our own shortcomings—particularly that of insufficient support for the patient in labor by "absent treatment." All of you have observed how the timely arrival and constant presence of the attending physician often makes the difference between "psychogenic dystocia" and a steadily progressive, physiological labor; between the need for much or little antepartum analgesia. You have observed, too, that often the noisiest patients in labor and those receiving the largest amounts of drugs to subdue pain and consciousness are the ones left in the care of the house staff until they are "saddle-blocked," "stirruped," and "ready to go."

Routine lack of support during labor and routine denial of pain-relieving measures before and during delivery are equally culpable and equally capable of doing psychological harm. For anatomical or psychological reasons not every patient is suitable for drugless childbirth, nor is everyone a proper subject for conduction anesthesia or inhalation anesthesia. George Speck<sup>13</sup> put it aptly: "There is no routine method for caring for any individual for there is no 'routine' individual." The Natural Childbirth movement, despite many exaggerated claims, has already done a great service in curbing the demands of the laity for amnesia at all costs. It will serve us well to re-educate ourselves and our associates to introduce consistently a greater measure of human kindness and understanding. Our patients like Sacajawea, whose labors for physical or emotional reasons are tedious and whose pains are violent, will always need all that art and modern science can offer. Because remedial measures like analgesia have been abused is no valid reason for abandoning them completely. In his masterful presidential address, Jeffcoate,14 reviewing the place of forceps in modern obstetrics, showed how the indications for the use of this instrument have evolved through periods of use and abuse. He said: "Babies previously born dead with forceps are now being delivered alive by cesarean section, while stillborn as a result of spontaneous delivery are now extracted alive with forceps." Obstetrics must constantly be alert to search and re-search explored and as yet unexplored domains to find the safe, progressive route and to define the frontiers of both knowledge and ignorance.

We left Lewis and Clark at Mandan, North Dakota, after the third stage of Sacajawea's labor. It is regrettable that the *Journals* make no references to the details of the immediate puerperium. This is a sad omission by the "young squires" and it demonstrates to our young men today that the publication even of humble case reports may some day benefit posterity. It is unfortunate also that we do not know whether Sacajawea experienced a feeling of exaltation after her heroic efforts at natural childbirth. As we read between the lines, however, it is abundantly clear that she was a good and devoted mother to little Baptiste and that he in turn became a likable child. *Post hoc ergo propter hoc.* I shall leave psychologists to draw this inference if they wish!

How interesting and informative it would be for us to know if this child of nature also suffered from "maternity blues" and how early after delivery ambulation occurred. Fortunately, Engelmann has filled this gap in our knowledge. He learned that enforced ambulation immediately after delivery was common practice among Indian tribes "to facilitate the flow of the lochia; they think that should the woman lie in bed the blood would accumulate in the abdominal cavity and she must die." For this, if for no other beneficial reason, we should feel encouraged that our recent rediscovery of early post-partum ambulation still rests upon sound grounds!

One fact that the *Journals* of Lewis and Clark make incontrovertibly clear is that Sacajawea participated in an all-out "rooming-in" program. Lewis leaves little doubt about this in his description of the setup while they were encamped in winter quarters at Fort Mandan:

Capt Clark myself the two interpreters and the woman and child sleep in a tent of dressed skins. this tent is in the Indian stile, formed of a number of dressed Buffaloe skins sewed together with sinues. It is cut in such manner that when foalded double it forms the quarter of a circle, and is left open at one side here it may be attached or loosened at pleasure by strings which are sewed to its sides for the purpose. (April 7, 1805.)

Modern hospital architects and enthusiastic supporters of "rooming-in" arrangements in hospitals will be delighted to learn of this trustworthy evidence that lying-in and nursery facilities can in fact be successfully combined without radical changes in building codes! In such cosy surroundings our heroine and her infant roomed-in for two months until the expedition again set out on its journey to explore the Yellowstone River.

On this trip, too, they "roomed-in" aboard the "White Perogue," a large canoe, sharing its close quarters with Lewis, Clark, "three men who could not swim," and father Charbonneau who also could not swim. It can be assumed that mother and baby here enjoyed some measures of comfort, if not physical security and privacy. As the canoe floated on the rivers, propelled by the wind, paddles, or by tow lines, the peace and quiet of the quarters provided ideal surroundings to pursue a regimen of "rooming-in" and "demand feeding." Sacajawea's life was a simple one and her demands for creature comforts were modest. "If she had enough to eat," wrote Lewis, "and

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a few trinkets to wear I believe she would be perfectly content anywhere." Small wonder that our squaw was still nursing her papoose successfully when the expedition ended 19 months and many adventures later.

If we contrast this idyllic environment and the Indian mother's bovine disposition to the hospital surroundings and psychological make-up of the modern Sacajawea, recent experiments in restoring natural, homelike methods of postnatal care to maternity units would seem to be beset with stupendous obstacles. Consider, if you will, the peace and quiet of a canoe trip marred only by the lapping of the waves, the splashing of paddles, the singing of birds, and the conversation of her male companions—frontiersmen were said to be remarkably taciturn! For the Mrs. Sacajawea of today the best-regulated hospital corridor is a midway of noise and confusion.

Beginning with the all-awake signal just after dawn, the time-honored hospital routine for the "lying-in" woman begins with enforced, self-administered early ablutions, needed or not. Then the morning "T.P.R." is taken by a night nurse anxiously waiting to publicize these scientific observations before filing the "Night Report" and departing for a much-wanted rest. Closely following is a welcome, though often hectic, encounter with her baby in an attempt at breast and/or bottle feeding. Then, the morning medicine, with or without enema, dutifully administered by a day crew still yawning or excessively exuberant, while the corridors outside the room resound with the clumping of tramping feet. By the time the breakfast tray arrives to provide the strengthening effect of a cup of coffee (if it is still warm) the modern Sacajawea already yearns for the next night's sleep.

But the day is not over. The maid who arrives to mop the floor and remove the breakfast dishes and the man with the infernal machine who polishes the corridor to the big front door, the doctor who pops in unexpectedly to make a brief call, and the endless chantings on the loudspeaker outside the door convince her that she is indeed being lavished with attentions and all's well in the whirl. This is particularly true if she has the added benefit (in a private room) of incoming telephone calls from her husband before he leaves for the office after a well-deserved night's rest and, later, the solicitous inquiries from her sisters, her cousins, and her aunts.

All these advantages of civilization plus bedside radio or even TV should make hospital life a constant round of pleasure for the mother if it were not for the repetition of scheduled baby feedings at four-hour intervals, afternoon visitors, frequent urgings to ambulate more freely, and, in the evening, the crowning joy of a visit with her husband who, poor lamb, works so hard and has had such a time supervising the household and 4-year-old Jimmy who is raising Cain with Grandma and won't eat!

Yes, Mrs. Sacajawea today has the best of everything! Not the least is the nice high hospital bed which is more convenient for the nurse to work at, "in case you should get some bed care, my dear!" From this lofty perch she must leap like a gazelle even if it hurts, you know where. Then, too, there is under the bedsheet the nice rubber or plastic cover for the sagging mattress

which keeps her moist and warm during the phase of postpartum diaphoresis. Postpartum diuresis, of course, is no longer a problem since we allow early ambulation and bathroom privileges down the hall and to the right. Modern Sacajawea wonders how her ancestors had the nerve to call this the "lying-in" period.

To all these rest-less routines of the modern hospital day some would now add the inovation of doing away with the rigid four-hour feeding schedule for the baby. In its stead they recommend keeping the baby in her room constantly and that she must feed him ad lib., with baths and diapering p.r.n. This is called "rooming-in." Note that while the baby eats ad libitum the mother will doubtless still be subject to the traditional hospital routine of a healthful fasting period from 5 or 5:30 in the afternoon until breakfast, unless the diet kitchen graciously supplements this fare with a jigger of juice or milk at bedtime!

This satirical account of hospital routines (which Dr. John Parks<sup>15</sup> presented with greater restraint) is not intended to discredit the altruistic motives of those who are currently experimenting with rooming-in programs. Rather, it is offered to suggest that perhaps there is a need for more such experiments to test whether still other traditional hospital routines might safely be modified or discarded. The beneficial effects of early ambulation, as an example, could not have been gained without courageous defiance of the old lying-in tradition. I ask you where we would be today if this primitive Indian practice had not been re-explored before these times of nurse shortages, almost 100 per cent institutional care for obstetrics, and rapid patient turn-overs enforced by inadequate hospital facilities in most communities? Despite many obvious advantages, however, early rising and early ambulation have commonly been misconstrued to mean minimal bedside attention, all too early release from the hospital and, in consequence, limited opportunity for relaxation unless Sacajawea is fortunate enough to have a home and relatives to provide her a "real rest" away from antiseptic routines. Our former President, Norman Miller, 17 has written eloquently about "Shortcomings in Puerperal Care," and has demonstrated in his own maternity service how many traditional routines may be safely discarded or minimized to provide some measure of added rest.

It is hard to see how rigidly enforced rooming-in routines will provide more rest and relaxation unless the hospital stay is prolonged beyond the usual six or seven days and unless a lot of other disturbing features are removed to compensate for the added responsibilities and work of caring for her baby. While "labor" is no longer necessarily synonymous with "ordeal," all will agree that it is a strenuous physical act which afterwards deserves rest and freedom from responsibility. In his classic Rest and Pain, Hilton long ago demonstrated the importance of rest for healing and established it as a major surgical principle. In our efforts to find ways and means of improving and expediting maternity care this fundamental principle seems to have been slighted. With early rising, early ambulation, early release from the hospital, and, now, complete care of the baby with relentless demand feeding "she is troubled," says the doctor in Macbeth, "with thick-coming fancies, that keep her from her rest."

If there is anything to be gained from these experiments in maternity care for the praiseworthy purpose of improving human relations, it appears to be the demonstration that other time-honored traditions and concepts may not be as valid as we believe. If, as the studies of complete and partial rooming-in programs by Parks and Montgomery<sup>16</sup> and others seem to show, rigid nursery isolation techniques are not quite essential for the normal newborn, perhaps other less vital routines for the mother could also be curtailed. It might be well for all of us to scrutinize standing orders on postpartum floors to see how many have been scheduled more to fit the patient to the hospital rather than to fit the present-day needs of the patient. I am sure that many could be rescheduled or omitted without seriously harming the working efficiency of the institution.

Only the early-rising Spartans among us will see merit in waking the patient at dawn for temperature determinations, medications, and baths in lieu of another hour or two of sleep before breakfast. Many mothers would welcome another forty winks by having their bottle-fed infants fed by the nursery staff at 2 and 6 A.M., certainly during the first few days of hectic, indifferent feeding. It might be revealed that many other treatments: antiseptic perineal sprays, routine medications and temperature determinations during the day, are quite unnecessary for the majority of healthy women, thus leaving more time for the staff to care for those who are really ill. The postwar innovation of midmorning and midafternoon "coffee breaks" for hospital personnel might, with equal justice, be made available to the hardworking postpartum convalescents. Parks suggested also that "an afternoon period of rest should be provided in which the patient is not disturbed by physicians, visitors, or incoming telephone calls." This would be a most welcome and desirable rule on most maternity floors. All these are small things, to be sure, but the sum total may add considerably to the strength and recovery of the patient.

Whether rooming-in programs really provide a more homelike, natural environment and whether healthier mothers and babies (physically and emotionally) will result remain to be seen. Certainly, no rigid, inflexible plan can be expected to succeed always since, to quote Speck again, "there is no 'routine' individual." Not all mothers automatically recover in the same manner from the effects of labor, react identically to the role of motherhood, or manifest the same capacity and desire for breast feeding. It is interesting to note in this connection that fewer private patients on Montgomery's service "accept" rooming-in, thus indicating, perhaps, that Sacajawean temperaments are not as prevalent in the "carriage trade."

Of the many controversial features of rooming-in perhaps the greatest criticisms can be leveled at the extravagant claims made by psychiatrists who promote these practices in the interest of emotional well-being of mother and child. However intriguing and plausible many of their speculations concerning the psyche may be, it must be admitted that all are not necessarily founded on objective evidence. It is highly questionable that many mothers have been

emotionally blighted because they did not experience the gratification of a conscious expulsion phase at delivery or that their children felt forever rejected because their mothers accepted an amnesic drug during labor. Similarly, it is hard to conceive that an infant becomes emotionally maimed because it spent lonesome hours in a central nursery and was cuddled only at four-hour intervals while being fed from breast or bottle. To mothers who have been unduly impressed by such psychiatric theories preached as facts great psychologic harm may be done by engendering feelings of inferiority in those who fail to measure up to the psychiatrists' code for normal behavior. While there is much need for scientific psychology in obstetrics, it appears that such words as "emotions," "rejections," "frustrations," and "psychic trauma" have been bandied about, perhaps a little too freely, in some quarters. Even the word "psychosomatic" in many instances seems to have become a wastebasket (like the old term, "idiopathic") in which to gather the symptoms for which an organic basis is not readily discernible or, often, not earnestly sought. The overzealous concern with emotions in some quarters reminds me of the quip of the cattleman from the Central States when the subject of "breeding" had been belabored by a Proper Bostonian: "We think breeding is a lot of fun but we don't think it is everything"!

When the Lewis and Clark Expedition reached the region of Great Falls, Montana, now the home of our benign President-Elect, Frank McPhail, they discovered the Marias River. The Indians had named this noisy, turbulent stream "The River That Scolds All the Others." At the risk of wearying you with further scoldings I wish to add one bit of criticism of the extremist "self-demand feeding" pediatricians whose interest in the baby often causes them to forget that mothers, too, are human beings. The report of an early enthusiast for nonscheduled breast feeding glowed (sadistically it seemed to me) because the rooming-in mothers nursed their babies as many as seventeen times per day in addition to unlisted numbers of diaper changes, also on demand. The numbers of cracked and infected nipples and breast abscesses were not recorded. It is interesting to read also that the babies gradually decreased their efforts day by day until two weeks later (possibly through sheer fatigue) they voluntarily selected a traditional four-hour schedule.

Unreasonable and inflexible insistence upon "demand feedings" of the foregoing type right from the start, certainly during the first few days of life when both mother and baby are still recovering from the effects of labor, seem physiologically unsound. If nourishment is so all-essential for the newborn child it seems likely that Nature would have provided for an abundant supply of breast milk immediately post partum instead of some days later. It seems paradoxical, too, that at birth babies are often pounded unmercifully to induce crying and pulmonary expansion, but during the ensuing days whenever they attempt by crying to reduce residual atelectasis the energetic demand feeders discourage this by offering milk instead of the oxygen they may be striving for! Is it a brash presumption to suggest that all infant crying is not from hunger or pain and that every crying babe need not automatically be fed or consoled?

Also, it is not easy to go along with the psychiatric trend of thought intruded into the demand feeding concepts and adding to parental anxieties that to deny a crying child a draught forbodes emotional instability in later life. I confess to being enough of a martinet to believe that the "spoiled child" is more often the result of being indulged too freely rather than not enough. No need exists to belabor this point unduly, since indications are that the extreme views of the demand feeders, child psychologists, and "progressive educators"-with their doctrines of permissiveness-have reached their limits and that a healthy turning of the tide is occurring. When his party was about to cross the Great Divide in 1805, Lewis recorded some interesting observations on child psychology as practiced by Sacajawea's people, the Shoshones or Snake Indians. He wrote, "They seldom correct their children particularly the boys who soon become masters of their own acts. they give as a reason that it cows and breaks the sperit of the boy to whip him, and that he never recovers his independence of mind after he is grown. They treat their women but with little rispect, and compel them to perform every species of drudgery."

As far as I can ascertain, the overindulged, permissively-reared Shoshone braves did not become men of distinction. Only Sacajawea is commemorated today in verse and prose, in paintings and statues and on postage stamps as a model of fortitude and human worth. Without faltering or complaining she carried her infant in a rawhide shoulder pack and cradle to the Pacific and back again. Certain child psychologists of today who are urging modern women to revive this method of carrying babies should note this historic fact to support their theory of an added means of building intimate mother-child relationships!

It was not far from the confluence of the Willamette and the Columbia Rivers that the Expedition first encountered tidal waters. This was at first a joyful experience since it showed that their long-sought destination, the Pacific Ocean, could not be far distant. Soon it became evident that the last was to be one of the most perilous phases of the adventure. The violent ebbs and floods brought added dangers and discomforts. The transition from fresh to salt water deprived them of drink but provided the opportunity for replenishing their salt stores. Had they been modern clinicians they would have observed the analogy between the perils of the low-salt syndrome and the equally ominous consequences of sodium and chloride excesses.\*

The ebbs and floods of the Pacific tides have analogies also in the currents and countercurrents in obstetrics which I have attempted to portray today. Just as the violent surges of sea waters upon the shore may shake moorings and bulwarks they also may bring to the land much that is new—even sunken treasures with mere flotsam and jetsam. Again, as the tide waters sweep back to the sea they carry away bits of dry and lifeless vegetation, pieces of

<sup>\*</sup>Clark wrote, November 9, 1805: "... notwithstanding the disagreeale Situation of our party all wet and cold (and one which they have experienced for Several days past) they are chearfull and anxious to See further into the Ocian, The Water of the river being too Salt to use we are obliged to make use of rain water. Some of the party not accustomed to Salt water has made too free a use of it on them it acts as a pergitive."

Later he added: "salt water I view as an evil in as much as it is not helthy."

driftwood, and some of the very land itself. With each ebb and flood something is lost and always something is added. So we may regard the new developments in obstetrics which I have presented today as resurgences often of previously abandoned practices. After the froth and the fury of the outgoing tide, a rare, though tiny, pearl may be uncovered among the dry shells upon the shore. Thus, poetically, we may consider natural childbirth, rooming-in, demand feeding, and other subjects we are looking upon today as tides in maternity care which doubtless will recede, but with equal certainty will leave as their sequel some benefits, perhaps only a greater humanity, in our professional lives.

The literary pursuit which I have just reported was not written; rather, as Proust said of one of his works, it was harvested. Many of those present will recognize their own views and opinions which I have borrowed freely to build my theme. Montaigne put it more clearly: "I have gathered a posie of other men's flowers and nothing but the thread that binds them is my own." In closing I am reminded uncomfortably also of a fitting verse from Ecclesiastes: "For a dream cometh of a multitude of business, and a fool's voice is known by the multitude of words."

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### THE ETIOLOGY OF CEREBRAL PALSY\*

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THE subject which I have chosen to lay before you, the etiology of cerebral palsy, is one which is rarely discussed in obstetrical circles. The vast literature of our specialty scarcely mentions it and, as far as I can ascertain, not a single paper dealing with this topic has hitherto been presented by an obstetrician before an obstetrical society in this country. Our almost complete neglect, as obstetricians, of the causation of this tragic disease, a disease which brings daily heartache to more than half a million parents throughout our land, is a surprising circumstance for a number of reasons.

In the first place, whereas our obstetrical literature rarely mentions cerebral palsy, the literature of cerebral palsy abounds with statements that the etiology of the disease is chiefly obstetrical. Thus, the very first paper on the condition published in 1853 by the English orthopedic surgeon, William John Little, was entitled "The Influence of Abnormal Parturitions, Difficult Labors, Premature Births, and Asphyxia Neonatorum on the Mental and Physical Condition of the Child, Especially in Relation to Deformities." During the hundred years which have elapsed since the publication of Little's classic paper, the preponderance of opinion has continued to lean toward the viewpoint that parturition is an important causative agent, the most prevalent idea being that the disease is usually due to mechanical trauma suffered by the infant's brain in the birth process. For example, Cecil's Textbook of Medicine makes the following statement: "The term 'Little's disease' is not now so commonly used, since it is not a pathologic entity, but is usually applied to cases of congenital spastic paralysis in children who have sustained some form of cerebral birth injury. Indeed, it also applies to cases of injury to the spinal cord during delivery, causing spasticity of the legs because of damage to the motor pathways in the spinal cord. The cerebral pathology may be due to spontaneous cerebral hemorrhage at the time of birth, to cerebral anoxia during birth or to damage from forceps." Most works on the subject discuss etiology even more briefly with such terse statements as, "The cause is usually obstetrical," or "Most cases are due to birth injury."

The emphasis which has been laid and is today laid on obstetrical factors in the causation of cerebral palsy is well illustrated by the classification of the disease, according to etiology proposed by the American Academy of Cerebral Palsy, a select body composed of recognized authorities on the subject. As shown in Table I, this classification cites prenatal factors as responsible for approximately 30 per cent of all cases and natal factors as responsible for about 30

<sup>\*</sup>Address of the Guest Speaker, presented at the Twenty-second Annual Meeting of the Central Association of Obstetricians and Gynecologists, St. Louis, Mo., Oct. 7 to 9, 1954.

per cent, the opinion of the American Academy of Cerebral Palsy being, therefore, that some 60 per cent of all cases are attributable to obstetrical factors. Since all authorities agree that the disease is rarely hereditary, the implication is that its genesis stems from faulty environmental conditions of one kind or another which develop sometime between conception and birth. Postnatal factors, it may be noted, were thought responsible for less than 10 per cent of all cases, while in 30 per cent no specific causative factor can be demonstrated.

Table I. Classification of Cerebral Palsy According to Etiology, Proposed by the AMERICAN ACADEMY OF CEREBRAL PALSY

I. Prenatal F	actors (Responsible for Approximately 30% of All Cases).—
1. Hered	litary (rare)
2. Acqui	red in utero
	enatal infection—toxoplasmosis, rubella, other maternal infection
b. Pr	enatal anoxia-carbon monoxide, or strangulation of mother, maternal
an	emia, hypotension, e.g., following spinal anesthesia, placental infarcts, or
ab	ruptio placentae, kinking of the cord
c. Pr	enatal cerebral hemorrhage—maternal toxemia, direct trauma, maternal
	eding diathesis

- d. Rh factor-kernicterus due to the Rh factor
- e. Metabolic disturbance—diabetes f. Gonadal irradiation-harmful exposure to x-ray

### II. Natal Factors (Responsible for Approximately 30% of All Cases).—

- - a. Mechanical respiratory obstruction
  - b. Atelectasis
  - c. Narcotism (due to drugs)
  - d. Placenta previa or abruptio placentae
  - e. Maternal anoxia or hypotension
  - f. Breech deliveries with delay of the aftercoming head
- 2. Cerebral hemorrhage and contusions
  - a. Traumatic-dystocia, disproportions and malposition, injudicious application
  - of forceps, holding back of head, pituitary extract induction of labor Sudden pressure changes—precipitate or cesarean deliveries, constitutional factors (prematurity)
  - c. Bleeding tendency-hypoprothrombinemia, anemia of the newborn

### III. Postnatal Factors (Responsible for Less Than 10% of All Cases) .-

- 1. Trauma—subdural hematoma, skull fractures, wounds and contusions of the brain (accidental)
- Infections—(more common in children than in adults) meningitis, encephalitis, brain abscess
- 3. Toxic causes—lead, arsenic, coal-tar derivatives
- Vascular accidents—(more common in adults than in children) aneurysms of circle of Willis, hypertensive encephalopathies, emboli due to bacterial endocarditis or fat embolism, cerebrovascular thrombosis in debilitated infants, sudden pressure changes
- 5. Anoxia—carbon monoxide poisoning, strangulation, high altitudes, and deep pressure anoxia, hypoglycemia
- Neoplastic, or late developmental defects-brain tumors, brain cysts, internal hydrocephalus, hydrocephalus
- IV. Unknown causes (Approximately 30% of All Cases)

Table I also lists the specific conditions which, in the opinion of the American Academy of Cerebral Palsy, are the main causes of the disease. Coming as they do from an authoritative body, these lists of obstetrical conditions are imposing, but it should be noted that they have been prepared largely on a presumptive basis, and that they lack any specific documentation. In other words, these are lists of conditions which, on the basis of theoretical reasoning, might be presumed to cause cerebral palsy.

Here, accordingly, is a disease which neurologists, pediatricians, and indeed all authorities agree is chiefly obstetrical in etiology. Is it not a strange paradox, then, that obstetricians have given the subject so little thought? This circumstance becomes all the more surprising when it is noted that, except for the single factor of premature birth, documentary evidence for or against the obstetrical hypothesis is very scanty.

The obstetrician's neglect of this problem is also surprising in view of its magnitude. As shown in Table II, the number of cases of cerebral palsy in the United States, based on the authoritative estimates of Phelps, is in the neighborhood of 350,000. The United Cerebral Palsy Association puts the figure somewhat higher at 550,000. Approximately one-third of these children have such serious impairment of their intellectual faculties that any program of effective training is out of the question; another one-sixth are so completely crippled as to make habilitation from the viewpoint of self-help or locomotion impossible. On the basis of Phelps' data and a population of 160,000,000, it is possible to estimate that the number of infants born in the United States each year who later develop cerebral palsy is roughly 11,200. Employing the same data and assuming that the birth rate is nearer 20 per thousand, it is also possible to estimate that about 3.5 such infants are born per 1,000 births. Levin, Brightman, and Burtt, on the basis of a study made in Schenectady County, New York, report a figure of 5.9 cases of cerebral palsy per 1,000 infants born who survive one month. To translate these figures into terms which can be readily appreciated by obstetricians, any obstetrical service which delivers 3,000 infants a year probably turns out 10 to 18 infants annually who later develop cerebral palsy.

TABLE II. INCIDENCE OF CEREBRAL PALSY IN THE UNITED STATES

1.	Total C.P. cases (Phelps)	336,000
2.	Infants with C.P. born annually per 100,000 population (Phelps)	7
3.	Total infants with C.P. born annually (calculated from No. 2)	11,200
	Infants with C.P. born per 1,000 births	,
	(Calculated from No. 2 on basis of 20 per 1,000 birth rate)	3.5
5.	Infants with C.P. born per 1,000 births	
	(Levin, Brightman, and Burtt)	5.9

The few studies which have been made on the etiology of cerebral palsy have suffered from lack of specific, complete, and detailed obstetrical information. Some have been based on the mothers' recollections as to whether the labor was long or difficult, whether instruments were used, and whether the baby was "blue" at birth. Others have gone back to the records of various hospitals at which the birth took place; but since the birth records of most hospitals are notorious for their brevity, stating in many instances merely the information necessary for the birth certificate, it is understandable that obstetrical information obtained in this way must be very skimpy and perhaps unreliable as well. In the outstanding study by Lilienfeld and Parkhurst on factors of pregnancy and labor associated with cerebral palsy, the authors reviewed the birth certificates of 561 children with cerebral palsy observed in a certain area of New York State. Since in that state the birth certificate provides a list of various obstetrical complications to be checked, such as breech presentation, placenta previa, toxemia, etc., the authors were able to bring out many important facts,

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especially the high incidence of abruptio and placenta previa in their series. But, at best, the information afforded even by the New York State birth certificates is inadequate to give a complete obstetrical picture; and some of the diagnoses may be open to question.

It is the purpose of the present communication to report an analysis of the obstetrical records of 96 infants who developed cerebral palsy. All these infants were born at the Johns Hopkins Hospital where our case histories provide a fairly complete and detailed picture of the whole course of pregnancy, labor, and the neonatal period. The 96 cases of cerebral palsy were culled from various Maryland cerebral palsy clinics and hospitals. The hospital where the baby was born was then ascertained, either through the records of the clinics or hospitals visited, or more often through the municipal office of vital statistics. As stated, only those infants who were born in our hospital were included in the series. The diagnosis of cerebral palsy had been made by specialists in this field as well as the type of neurological disorder present. In order to provide a basis for comparison, a control series of 11,195 infants who were born in our hospital between 1945 and 1949, and who survived, has been analyzed in respect to the same complications encountered in the cerebral palsy series. This period of time was chosen because most of the infants with cerebral palsy in the study were born during these years.

TABLE III. CONDITION AT BIRTH OF 96 INFANTS WHO LATER DEVELOPED CEREBRAL PALSY COMPARED WITH CONTROL PERCENTAGES

CONDITION AT		C.P. SERIE	ES	1	CONTROLS
BIRTH	FULL TERM	PREMATURE	TOTAL	PER CENT	PER CENT
Good	34	14	48	50	87
Fair	4	5	9	9	11
Poor	24	15	39	41	2

If there is any question about the importance of obstetrical factors in the etiology of cerebral palsy, it will be dispelled by a study of Table III. It is routine in our hospital to record on the labor chart the condition of the baby at birth by encircling one of four printed words on the chart in the section dealing with the newborn. These words are: "Good," "Fair," "Poor," "Dead." This designation on the chart states the clinical impression of the attending obstetrician or pediatrician of the condition of the baby as attested by its behavior during the first hour of life. This fact needs emphasis because in going back to the obstetrical histories of these infants with cerebral palsy it should be made plain that we did not read into those histories any observations that had not been clearly recorded there at the time of birth. As shown in the last line of Table III, the word "Poor" was encircled in 41 per cent of the cerebral palsy series in contrast to 2 per cent in the control group. The reason for calling the condition of such a large number of babies "Poor" at birth was most frequently abnormalities of respiratory behavior, but in some cases it was flaccidity, cyanosis, and the character of the cry. Most often a combination of these findings dictated placing the infant in this group. The fact that many of the babies in the cerebral palsy series had already suffered severe damage prior to birth is revealed also by the breathing time of these infants as shown in Table IV.

Breathing times under two minutes showed about the same frequency in the cerebral palsy series and in the controls, but the extremely high incidence of very prolonged breathing times in the cerebral palsy group is evidenced by the inordinately large proportion of these infants who showed a breathing time of more than two minutes. Most noteworthy perhaps is the fact that 13 per cent of the babies who developed cerebral palsy did not breathe spontaneously for six minutes or more, whereas such an extremely long breathing time was observed in the controls only once in about 300 cases. Further evidence that the cerebral palsy infants were gravely handicapped at the time of birth is shown by the prolonged duration of their hospital stay. The hospital stay of premature babies depends chiefly on the degree of prematurity and is not necessarily an index of their state of well-being over the neonatal period. On the other hand, the average stay of mature babies in our hospital, as shown by the control series, was 5.3 days and, with rare exceptions, any appreciable prolongation in the stay of mature babies is indicative of difficulties of one kind or another. The average stay of the 62 mature babies in the cerbral palsy series was 15.1 days. The pediatric records show that the conditions which most frequently necessitated such prolonged hospitalization were abnormal respiratory behavior, repeated attacks of cyanosis, feeding difficulties, prolonged, unexplained fever, and failure to gain in weight. Strangely enough, neurological signs and symptoms were encountered less frequently than the findings just mentioned, only 5 infants in the entire series of 96 showing actual convulsions. In sum, about onehalf of the cerebral palsy infants showed clear-cut evidence of having sustained some form of intrauterine injury either shortly before birth or early in the antepartal period.

TABLE IV. BREATHING TIME AT BIRTH OF 87 INFANTS WHO LATER DEVELOPED CEREBRAL PALSY (NOT RECORDED IN 9 CASES IN SERIES)

		C.P. SERII	ES		CONTROLS
TIME	FULL TERM	PREMATURE	TOTAL	PER CENT	PER CENT
Immed 5 sec.	30	22	52	60	72.0
6- 29 sec.	7	2	9	10	14.7
30- 59 sec.	5	1	6	7	8.0
60-119 sec.	2	0	2	2	3.5
120-179 sec.	2	0	2	2	0.6
180-239 sec.	1	0	1	1	0.3
240-299 sec.	1	1	2	2	0.2
300-359 sec.	1	1	2	2	0.2
359 sec. plus	9	2	11	13	0.3

The question now becomes: What was the nature of this intrauterine injury? Was it traumatic? Was it anoxic? Or was some other circumstance responsible? Or, were some combinations of these factors at work? In attempting to answer these questions, let us first mention a few conditions which, in our experience, do not cause cerebral palsy. An analysis of the obstetrical records of our 96 cases indicates that race, age, parity, syphilis, virus infection in the mother, type of pelvis, and total duration of labor show no significant correlation with the subsequent development of the disease. Nor did our data reveal that Rh immunization plays any important role, since the incidence of Rh negativity in these mothers was only 15 per cent, a figure not significantly higher

than in the control series. Three infants in the 96 showed pronounced jaundice in the early neonatal period, it is true, but in all 3 of these cases the mother was Rh positive. Hence, there was no case in our study in which Rh immunization could be incriminated. Beyond all question, erythroblastosis can cause cerebral palsy, particularly through the agency of kernicterus, but the evidence at hand would suggest that it is an uncommon cause and that it is responsible for no more than 2 or 3 per cent of all cases.

The distribution of the various neurological types of cerebral palsy, as established by competent specialists, is shown in Table V. When broken down into these very small groups the figures do not lend themselves to statistical analysis, but as far as we could ascertain there was no relationship between the neurological type of the disorder and any particular obstetrical complication.

Table V. Distribution of 96 Cases of Cerebral Palsy by Neurological Type and Premature Birth

TYPE	PREMATURE	FULL TERM	TOTAL
Spastics	30	56	86
Diplegia	10	30	
Hemiplegia	7	13	
Paraplegia	8	8	
Double hemiplegia	. 5	5	
Flaceid	2	5	7
Rigid	1	1	2
Ataxic	1	0	1
Total	34	62	96

Incidence of premature birth: 35.4% (clinic incidence: 9.2%).

The most generally known and best attested etiological factor in cerebral palsy is premature birth. The bottom line of Table V shows the very high incidence in the present series, that is, 35 per cent, or about six times the usual incidence of premature birth in our hospital. From the time of Little on, all series of cases of cerebral palsy have shown an extremely high incidence of premature birth, in the neighborhood of 30 to 40 per cent; and this is the one etiological factor, and possibly the only one, which has been established beyond peradventure. But the question has been raised as to whether the factor to be incriminated in these premature cases is the premature state of the infant per se or certain complications which we know predispose to premature birth, especially abruptio placentae and placenta previa. In the present series of 34 premature births, a pathological degree of uterine bleeding (that is, definitely more than "show" occurred in the last half of pregnancy or in labor in 11 instances, or about one-third. There were 2 cases of outright abruptio. figures for bleeding in the last half of pregnancy and for abruptio are several times the usual clinic incidence, and there can be no doubt that in many cases of premature birth the placental separation and subsequent anoxia are responsible for the cerebral damage rather than the prematurity per se. On the other hand, in 23 of our premature births, no abnormal bleeding occurred in the last half of gestation or in labor; and the evidence indicates that in this large proportion the subsequent development of cerebral palsy was in some way attributable to the prematurity itself.

TABLE VI. INCIDENCE OF VARIOUS DEGREES OF PREMATURITY IN 34 CASES IN WHICH THE INFANT DEVELOPED CEREBRAL PALSY

	C.F	. CASES	CONTROLS
WEIGHT GROUPS	CASES	PER CENT	PER CENT
1,000-1,499 grams	8	23.5	12.4
1,500-1,999 grams	8	23.5	20.1
2,000-2,499 grams	18	52.9	67.5

Table VI explores the role of prematurity in cerebral palsy still further and presents suggestive evidence that the degree of prematurity increases the likelihood of cerebral palsy. Thus, a disproportionately large percentage of very small infants (between 1,000 and 1,500 grams) were encountered in the cerebral palsy series, twice the number met in the control series. These data are just on the border line of statistical validity and should be interpreted merely as indicating a trend with a one-in-twenty chance of sampling error. In passing it may be noted that among the 8 infants in the 1,000 to 1,499 gram group, 3 developed retrolental fibroplasia in addition to cerebral palsy.

One of the more noteworthy observations in the present study was the frequent association of sepsis, intrapartum and neonatal, with the subsequent development of cerebral palsy. Table VII brings out the fact that intrapartum fever was seven times more common in the mothers of the cerebral palsy infants than it was in the control series. But even more striking is the observation that prolonged neonatal fever (100° F. for three or more days) was three hundred times more common in the cerebral palsy infants than in the controls.

TABLE VII. INCIDENCE OF SEPSIS, INTRAPARTUM AND NEONATAL, IN 96 CASES IN WHICH THE INFANT LATER DEVELOPED CEREBRAL PALSY

	1	C.P. CA	SES		CONTROLS
	FULL TERM	PREMATURE	TOTAL	PER CENT	PER CENT
Intrapartum fever	7	2	9	9.4	1.3
Neonatal fever, transient	5	5	10	10.4	4.8
Neonatal fever, prolonged	15	14	29	30.2	0.1

The statistical validity of these figures is so great that the chances against their being due to a sampling error are inconsequential. But at this juncture let us avoid a common pitfall and recall that statistical validity has nothing whatsoever to do with causation; and the mere fact that intrapartum fever and neonatal fever are associated with the subsequent development of cerebral palsy in a high percentage of cases does not mean necessarily that they cause the disease. Thus, as every obstetrician knows, intrapartum infection is most likely to develop in prolonged labors, in stubborn labors—indeed, in just the type of labor which may have to be terminated by a difficult midforceps operation or a difficult breech extraction; and it is quite conceivable in such cases that it is the trauma of delivery which causes the brain damage and that the associated infection has nothing to do with the matter. For example, in 2 of the cases of intrapartum infection, the mothers were referred to us after repeated but futile attempts at forceps delivery by general practitioners in the home; and the bruised, lacerated state of the birth canal in these women left no doubt that brute force was about the sole expedient employed. The fact that

these two infants subsequently developed cerebral palsy is clearly explained on the grounds of trauma and it seems probable that the associated infection had little or nothing to do with it. The significance of intrapartum fever in our present investigation must also be evaluated from another viewpoint. It is well established that for each degree of body temperature over 98.6° F., the oxygen required for tissue metabolism, including brain tissue, rises 7 per cent. In other words, with an intrapartum fever of 101.6° F., the infant's brain requires one-fifth more oxygen than it would at a normal temperature. This fact needs emphasis because in evaluating intrapartum infection as a possible cause of cerebral palsy, it must be remembered that it can act not only through the effects of bacterial toxins but also through the mechanism of anoxia just described.

As for the large number of babies who showed prolonged fever (100.0° F. for three or more days), it was impossible to ascertain with certainty the number of these infants in whom the fever was due to actual infection and in what proportion it may have been attributable to the aftereffects of trauma and/or brain hemorrhage. Moreover, it is conceivable that injury to the hypothalamus, either traumatic or anoxic, may have produced such disturbances in the heat-regulating center as to have caused aberrations of temperature. We must, therefore, be cautious in drawing conclusions from Table XI. Nevertheless, even after eliminating the complicating factors we have just discussed, even after eliminating labors of less than three hours and longer than twenty-four hours, even after eliminating all but easy deliveries—in other words, even after eliminating as far as we can the factors of trauma and anoxia, mothers with intrapartum fever still loom up five times more often, and babies with prolonged fever still appear two hundred times more frequently in the cerebral palsy group than in the control series.

It has long been known that cerebral palsy can be caused by infectious diseases occurring in infancy. Thus, cases following pertussis, measles, diphtheria, scarlet fever, pneumonia, and various toxic conditions of unknown origin have been reported in goodly number. It is also recognized by competent students of the subject that the younger the infant is at the time of the infection the more severe the aftereffects are likely to be. In view of the wide range of infectious processes which may give rise to cerebral palsy in infancy, there is reason to suppose theoretically that infections contracted in utero might produce similar results. The high frequency with which the cerebral palsy infants in our series showed a background of intrapartum or neonatal infection needs confirmation at other hands but we cannot escape the suspicion from our investigation that such infections may play a much greater part in the etiology of cerebral palsy than has hitherto been realized. If this be true, here is one sphere in which obstetricians can play a role in the reduction of this disease. The implication is, of course, that any degree of intrapartum or neonatal fever must be combated immediately by adequate doses of antibiotics.

The opinion is growing that anoxia, consequent upon varying degrees of placental separation, is an important, if not the most important, cause of cerebral palsy. The study already referred to by Lilienfeld and Parkhurst attested

to such a relationship, as did also an investigation of 61 cases of cerebral palsy studied in our clinic by Latham, Anderson, and Eastman. The present investigation gives further support to this concept; but as our studies have progressed it has been increasingly clear that it is difficult to establish in any clear-cut way the true incidence of bleeding in the control series. It is likewise difficult to determine with any degree of certainty the amount of blood lost. These are sources of error which must be given due consideration in any evaluation of bleeding in pregnancy as it pertains to the development of cerebral palsy. Nevertheless, the high frequency of bleeding after the twentieth week in the present series, as shown in Table VIII, plus the fact that there were 2 cases of abruptio in these 96 cases, indicates that placental separation with subsequent anoxia may be responsible for many cases of this disease.

TABLE VIII. INCIDENCE OF BLEEDING IN PREGNANCY IN 96 CASES IN WHICH THE INFANT SUBSEQUENTLY DEVELOPED CEREBRAL PALSY

	C.P. SERIES		CONTROLS
	CASES	PER CENT	PER CENT
Bleeding before 20 weeks	14	14.6	14.5
Bleeding after 20 weeks	21*	21.9	4.1
Bleeding some time in pregnancy	35	36.5	18.6

\*Includes two cases of abruptio.

Mechanical trauma is unquestionably responsible for a certain number of cases of cerebral palsy, but in present-day practice the role it plays is certainly much less than was hitherto thought. Table IX shows clearly that some of our cases were caused by mechanical trauma. Thus, the infant in one case weighed 5,000 grams at birth, gave great difficulty in the extraction of the shoulders, and did not breathe for 25 minutes. There can be no doubt what caused that case of cerebral palsy. It will be noted also that the frequency of breech and midforceps delivery was higher than in the control group. Prolonged second stages were also more frequent but whether these are to be incriminated on the grounds of mechanical trauma or on the grounds of anoxia it is impossible to say.

TABLE IX. INCIDENCE OF CONDITIONS CONDUCIVE TO MECHANICAL TRAUMA IN 96 DELIVERIES IN WHICH THE INFANTS SUBSEQUENTLY DEVELOPED CEREBRAL PALSY

	C.P.	CONTROLS	
CONDITION	CASES	PER CENT	PER CENT
Breech delivery	8	8.3	3.2
Midforceps	6	6.3	2.0
Shoulder dystocia*	3	3.2	0.3
Second stage over 3 hours	7	8.1†	2.9

\*Includes one 5,000 gram infant; breathing time 25 minutes.

†Based on 86 cases; data not available in 10 cases.

As shown in Table X, the incidence of malformations in the series of cerebral palsy cases was much higher than in the controls. These malformations ranged from very minor defects, such as supernumerary digits, to more serious malformations, such as cleft palate and harelip. These findings suggest that a certain minority of cases of cerebral palsy are due to derangements in embryological development but whether these are genetic or environmental cannot be said.

TABLE X. INCIDENCE OF MALFORMATIONS IN 96 INFANTS WHO DEVELOPED CEREBRAL PALSY

	C.P. CASES		CONTROLS
	CASES	PER CENT	PER CENT
Total malformed infants (major and minor)	14	14.6	3.8

Table XI lists a number of conditions pertinent to the present investigation. As might be suspected, fetal distress was noticed in labor almost four times more frequently in the cerebral palsy series than in the control group. view of the present interest in postmaturity, and more particularly its association with anoxia, it is worth while noting that postmaturity was no more frequent in our cerebral palsy series than in the control group. Surprisingly enough, prolapse of the cord showed no increased frequency over that in the control group. Four of the cerebral palsy infants were delivered by cesarean section but in 3 of these abdominal deliveries there had been prolonged rupture of the membranes, and in one case outright intrapartum infection. Since our clinic is a referral center for 55 prenatal clinics scattered throughout the State of Maryland, the incidence of toxemia is extremely high in our general clinic population, and this accounts for the 20.5 per cent figure in the control group. It will be noted that the frequency of toxemia in the mothers of the cerebral palsy infants did not appear to be appreciably higher than in the controls. anesthesia complications, both in the cerebral palsy series and in the control group, were comprised for the most part of vomiting and aspiration of vomitus, and falls in blood pressure with conduction anesthesia. Two of the mothers in the cerebral palsy series were in shock in connection with the anesthesia complication. It would be reasonable to believe that the graver types of anesthesia accidents, particularly when associated with maternal cyanosis and/or pronounced drops in blood pressure, might be responsible for a small minority of cases of cerebral palsy.

TABLE XI. MISCELLANEOUS OBSTETRICAL CONDITIONS OBSERVED IN 96 CASES IN WHICH THE INFANTS DEVELOPED CEREBRAL PALSY

1	C.P.	SERIES	CONTROLS
	CASES	PER CENT	PER CENT
Fetal distress	12	12.5	3.5
Postmaturity	8	8.3	7.3
Prolapse of cord	1	1.1	0.8
Cesarean section	4	4.2	4.6
Toxemia	24	25.0	20.5
Anesthesia complications	4	4.2	1.0

In summing up the various data which have been presented, it would be most gratifying and informative if we could assign to each complication we have mentioned a specific figure and say that precisely this proportion of cerebral palsy cases are due to prematurity, and that precise percentage to hemorrhage or to infection. But, unfortunately, these factors rarely act alone but synergize with one another so that three or four may be active in a given case without any rational basis for deciding which is the most culpable. It is possible, however, to make the following statement. All the 96 case histories were re-

viewed finally to determine how many of the mothers enjoyed a relatively normal pregnancy and labor. For the purpose of this study, the term a "normal pregnancy and labor" was defined as follows: no abnormal bleeding in pregnancy or labor, a labor lasting between three and twenty-four hours, a second stage of less than two hours, no intrapartum fever, a spontaneous or low forceps delivery by the vertex, no anesthesia complication, and a baby who weighed 2,500 grams or more at birth, and who remained afebrile during the hospital stay. Only 18 cases complied with these criteria. In the remaining 78, one or another complication was present, and often multiple complications.

If it be true that the majority of cases of cerebral palsy are of obstetrical etiology, what can be done about it? Something can be done and something is being done. I want now to close on the following practical note. The American Academy of Cerebral Palsy has recently asked the American Academy of Obstetrics and Gynecology to appoint a liaison agent to the end that the common interests of the two academies be brought closer together, and the obstetrical factors in the etiology of cerebral palsy be explored under the combined aegis, and with the combined resources, of both groups. The American Academy of Obstetrics and Gynecology has complied with this request and it seems probable that the following course of events will ensue. In the first place, the American Academy of Cerebral Palsy will be asked to promulgate the teaching that the case history of every infant with cerebral palsy should include the exact date of birth, the name and location of the hospital in which the baby was born, and, if possible, the name of the attending obstetrician or physician. Heretofore this has rarely been done.

In the second place, the American Academy of Cerebral Palsy will be asked to make this disease reportable in the following sense. Every cerebral palsy clinic and every specialist in the field will be requested to report all definitely diagnosed cases to the obstetrician who attended the mother or to the obstetrical clinic concerned. Heretofore, pediatricians and neurologists have been hesitant to report these cases to the obstetrician concerned because the prevalent notion in regard to traumatic etiology carried with it certain unpleasant implications. We now know that trauma is an uncommon cause of cerebral palsy, and obstetricians should welcome the opportunity to study the obstetrical records of these cases objectively and without any sense of culpability. If this plan of reporting cases of cerebral palsy can be developed effectively, some of our larger obstetrical clinics could probably report within five years a larger series than I have analyzed this morning.

In the third place, provided that this system of reporting is successfully maintained, the American Academy of Obstetrics and Gynecology will be asked to establish a cerebral palsy registry to which individual obstetricians, as well as clinics, can send the obstetrical records of their cerebral palsy cases for pooling and analysis. We need more data on the obstetrical etiology of cerebral palsy, because, with a full appreciation of the causative factors, we may be able to do much to prevent this tragic affliction. The 96 cases which I have reviewed here are too few in number to give a full picture. We need rather a series of 1,096 cases; and this will be possible if such a registry is established. I have reason

to believe that pediatricians, neurologists, and indeed the entire group of workers in the cerebral palsy field will cooperate fully. But it is equally essential that this program have the endorsement, the support, and the active help of obstetricians throughout the country. It is for this reason that I have had the temerity to lay before you this rather out-of-the-way subject.

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### HAEMOPHILUS VAGINALIS VAGINITIS\*

A Newly Defined Specific Infection Previously Classified "Nonspecific" Vaginitis

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DURING the past two or three decades a voluminous literature has accumulated on the subjects of vaginal trichomoniasis and moniliasis, and every physician practicing gynecology has become familiar with their clinical aspects. A third type of infection, commonly referred to as "nonspecific" bacterial vaginitis, has not received the recognition which its clinical importance appears to warrant. Medical literature contains conspicuously little on the subject, and textbooks contribute no more than a few lines to its discussion.

Although "nonspecific" bacterial vaginitis has continued to be attributed to a large and unrelated group of bacteria, the assumption has been accepted with obvious reluctance. An intensive search of the literature has failed to reveal a single reference incriminating any specific organism as etiological in more than a small percentage of cases. Hite, Hesseltine, and Goldstein¹ state: "Reported results are variable and difficult to correlate, undoubtedly owing in part to difference in material and in part to differences in cultural methods and criteria for identification of the isolated organisms." Bernstine and Rakoff² state: "Non-specific vulvovaginitis constitutes a diverse group of vaginal infections which cannot be attributed to any specific pathogenic organism." Weaver³ in a recent article states: "It hardly appears suggestive that any one or more types of bacteria have a cause-and-effect relationship to non-specific vaginal discharges."

Several bacteria are usually blamed in each individual case. Those most often mentioned are the various staphylococci, streptococci, coliform bacilli, micrococci, and diphtheroids.<sup>1-7</sup> That so large a group of unrelated bacteria would be capable of producing a vaginitis has seemed unlikely. If they had such common prepotency, it necessarily would be a rare coincidence that the resulting discharges would have identical physical characteristics as regards consistency, color, odor, and microscopic appearance. Bernstine and Rakoff² have aptly expressed themselves: "Indeed, in many instances the term 'nonspecific' vaginitis is a misnomer used glibly to conceal ignorance of the true underlying cause."

We are prepared to present evidence that the vast majority of so-called "nonspecific" bacterial vaginitides constitute a specific infectious entity

<sup>\*</sup>Presented as the prize award paper at the Twenty-second Annual Meeting of the Central Association of Obstetricians and Gynecologists, St. Louis, Mo., Oct. 7 to 9, 1954.

caused by a single etiological agent. It has been a long-standing observation of one of us (H. L. G.) that the majority of bacterial vaginitides show on microscopic examination solid fields of small pleomorphic gram-negative bacilli. During several years prior to the present investigation, vaginal material had been sporadically submitted to clinical laboratories for culture. The reports were extremely variable and in no way supported the contention that a single organism was responsible. A logical correlation could never be drawn between the culture results and the stained smears, a point which suggested that the organism in the smears was not appearing in the cultures.

The second author (C. D. D.), after being made acquainted with the apparent inconsistencies, was furnished material from a typical case of bacterial vaginitis for bacteriological study. Although microscopic examination showed the characteristic organism in large numbers, no growth was obtained on culture media. Material from a second case was submitted. This time a large variety of highly enriched media were used and incubations made under various oxygen and carbon dioxide tensions. At the end of 48 hours, a 10 per cent sheep blood agar plate, incubated under reduced oxygen tension, was found to contain thousands of minute transparent colonies which could be detected only by reflected light. A smear from these colonies showed bacilli similar to those seen on the direct smear.

After finding the identical organism in pure culture in 13 of the next 14 patients considered as having bacterial vaginitis, it appeared that a specific etiological agent had been found to explain the majority of "nonspecific" bacterial vaginitides. We have assigned the name *Haemophilus vaginalis* to the newly isolated bacillus.

### Materials and Methods

All clinical observations during this study were personally made by one of us (H. L. G.), and all bacteriological procedures were personally done by the other (C. D. D.). This rule was followed to ensure a uniformity of method and interpretation.

The patients studied included all 1,181 who came under observation during the period of the investigation. All patients were white and from the private office of one of us. Sexually active women constituted the large majority of the patients, but also included were a few children and postmenopausal women. The patients were divided into two groups: obstetric (602) and gynecologic (579).

Microscopic examinations of wet mounts and stained smears were made on all patients who had subjective symptoms of vaginitis, or who showed gross evidence of vaginitis on inspection. All patients with an abnormal discharge, considered vaginal in origin, who showed no trichomonads or Monilia by microscopic examination, were subjected to bacteriological studies. Sixtyone of 80 patients with smears positive for trichomonads, and 47 of 79 patients with moniliasis were also studied bacteriologically.

A group of 78 patients, clinically normal, as determined by physical characteristics of the vaginal secretions, was studied bacteriologically as normal controls. A miscellaneous group of 43 patients, including some with abnormal volumes of normal-type secretions, some with cervicitis, cystitis, abnormal bleeding, etc., was likewise studied bacteriologically and included as a control group.

All patients were instructed to discontinue douches for the duration of the study and to have intercourse only when a condom was used. Although preliminary microscopic studies were made when vaginitis was first suspected, the clinical, microscopic, and culture descriptions were generally those made after several days' abstinence from intercourse and douching (Table I). Initial posttreatment follow-up studies were made 10 or more days after completion of treatment.

TABLE I, THE INTERVAL SINCE DOUCHE AND/OR INTERCOURSE AND THE INITIAL BACTERIOLOGICAL STUDY OF PATIENTS WITH H. VAGINALIS

DA	AYS SINCE LAST INTERCOURSE OR DOUCHE	NUMBER OF PATIENTS
	1 or less	12
	2	14
	3	11
	4	13
	5 or more	91
	Total	141

The presence of odor was determined by smelling the secretions on the withdrawn speculum. This technique partially eliminated odors arising from the vulva

Hydrion paper was used for determining the pH. The accuracy of this method was checked, using the Beckman pH meter, and was found to be reliable for practical purposes. pH was usually taken from the right lateral fornix.

The technique for obtaining material for smears and culture was as follows: With the labia minora spread, accumulated discharges were wiped from the vestibule of the vulva with a large cotton swab. A boiled, unlubricated bivalve speculum was inserted for a short distance into the vagina. The upper half of the vagina was then exposed without contamination by spreading the blades of the speculum. Material for study was taken from the fornices ahead of the speculum. A cotton swab which had been sterilized in 0.8 ml. of thioglycollate broth was applied to the left fornix, removed without contamination, and then swirled in the broth remaining in the culture tube. Dry smears were prepared from material in either the anterior or right lateral fornix, and stained with Gram and Giemsa. Material for the wet mount was taken from the withdrawn speculum, mixed with a drop of normal saline on a slide, cover-slipped, and examined immediately. The wet mount was studied for the presence of trichomonads, Monilia, morphology of the bacteria, relative numbers of pus and epithelial cells, and the condition of these cells.

Material obtained for culture was received in the laboratory, usually within three hours after collection. This material was inoculated to the following media: Bacto proteose No. 3 agar (Difco) containing 10 per cent defibrinated sheep blood, incubated aerobically, in carbon dioxide (candle jar) and anaerobically; Sabouraud's dextrose agar (Difco), incubated at 20° C. and 37° C.; Bacto tomato juice agar (Difco), incubated in carbon dioxide and anaerobically; Bacto brain heart infusion broth (Difco); and thioglycollate broth, Brewer modification without indicator (Baltimore Biological Laboratories).

All cultures were examined at 24, 48, and 72 hours, and at 5 days. Broth cultures displaying turbidity were examined by gram-stained smears and subcultured to appropriate media for identification. Plates were observed by oblique lighting and all different types of colonies were examined by smears and subculture.

## Clinical Manifestations

The clinical manifestations of trichomoniasis and the physical characteristics of normal vaginal secretions provide a practical basis for a comparative description of H. vaginalis vaginitis (Table II). A normal vaginal secretion, exclusive of cervical mucus, is usually white and of a curdy consistency, resulting from the mixture of aggregations of epithelial cells in the serous constituent. The volume of normal secretions is largely dependent upon the hormonal status of the individual patient. The odor of the secretion, with a few exceptions, is not particularly disagreeable.

The volume of discharge from H. vaginalis infections varied from scanty to profuse, but was usually moderate, being somewhat less than in the average case of trichomoniasis. Many of the patients were actually unaware of a discharge, but "discharge" was the chief complaint in a large percentage of the infected nonpregnant group. Many of the obstetrical patients also had the incidental complaint. The majority of those denying discharge admitted "soiling" of the underwear.

TABLE II. CHARACTERISTICS OF DISCHARGES COMPARED

	H. VAGINALIS	TRICHOMONAS	NORMAL +	
Volume	++	+++		
Color				
Gray	85.%	46%	7%	
Yellow green	3	36	0	
Yellow gray	5	10	7	
White	7	8	86	
Odor	++	+++	<u>+</u>	
Frothiness	27%	34%	1%	
Consistency	Homogeneous	Homogeneous	Curdy	
pH	5.0-5.5 (91%)	5.0-6.0 (95%)	4.0-4.7 (92%)	

The color of the discharge was recorded as gray in 85 per cent, white in 7 per cent, yellow gray in 5 per cent, and yellow green in 3 per cent. For comparison, the discharges in 63 patients with positive Trichomonas smears were described as gray in 46 per cent, white in 8 per cent, yellow gray in 10 per cent, and yellow green in 36 per cent. Thus a yellow-green discharge almost invariably indicated trichomoniasis, rather than *H. vaginalis* vaginitis. Normal secretions were usually described as white.

The odor of the discharge is usually less offensive than that of trichomoniasis. In the 141 cases of *H. vaginalis* infection, the odor was described as disagreeable in 117 and offensive in 24. Practically all patients were conscious of a disagreeable odor. Normal vaginal secretions were rarely recorded as odorous.

Frothiness of the discharge was present in 27 per cent of the cases of H. vaginalis vaginitis and in 34 per cent of the cases of trichomoniasis. Frothiness, therefore, cannot be interpreted as being a characteristic peculiar to trichomoniasis.

The consistency of the discharge is relatively thin, being approximately of the same fluidity as the discharge of trichomoniasis. The discharge frequently shows a tendency to adhere to the vaginal wall in a thin film, instead of pooling in the posterior fornix. It has some resemblance to a thin flour paste, being turbid, but uniformly homogeneous, with an absence of gross clumps of epithelial cells. The discharge of trichomoniasis is likewise homogeneous, while the consistency of normal vaginal secretions is distinctly curdy.

The pH of the discharge: Ninety-one per cent of the discharges from H. vaginalis infection fell within a pH range of 5.0 to 5.5, with the extremes being 4.5 and 6.0. Ninety-five per cent of the discharges from trichomoniasis showed

a pH between 5.0 and 6.0. Ninety-two per cent of the normal controls showed a pH between 4.0 and 4.7. A pH of 5.0 or greater in a woman with functioning ovaries and with no trichomonads on wet mount was indicative of a bacterial vaginitis with *H. vaginalis* the most likely offending organism.

On *inspection* a minimal degree of redness or edema of the vulva was noted in 22 per cent and some evidence of minimal vaginal pathology as indicated by petechiae or redness was noted in 11 per cent. Thirty per cent had some cervical pathology such as erosion, cysts, polyps, or endocervicitis. Since essentially the same percentage of the normal controls had one of these findings, there appeared to be no important relationship between cervicitis and *H. vaginalis* infections.

Symptoms: The most common subjective symptom was itching or burning of the vulva. Thirty-one per cent admitted one of these symptoms but they were usually mild, and in no way comparable to the itching of Trichomonas and Candida albicans infections.

A side observation during this study was that many patients with clinically and bacteriologically normal vaginas answered affirmatively when directly questioned about vaginal irritation and/or itching, a fact which would seemingly lessen the significance of such symptoms in *H. vaginalis* vaginitis.

## Incidence

The relative incidence of the various infectious vaginitides encountered during the course of this study is given in Table III.

TABLE III. INFECTIOUS VAGINITIDES ENCOUNTERED IN 1,181 PATIENTS EXAMINED

Haemophilus vaginalis vaginitis—Total cases		141
Pure bacterial culture, one or more times	85	
With one or more other bacterial organisms—each culture	56	
With Monilia	7	
With Trichomonas	12	
Bacterial vaginitis (other than H.V.)—Total cases		11
Grade II flora	8	
Grade III flora	3	
Trichomonas (positive smear)—Total cases		80
Trichomonas (of 61 cultured) with Haemophilus vaginalis	12	
Candida (moniliasis)—Total cases		79
Moniliasis (of 47 cultured)—with Haemophilus vaginalis	2	
Granuloma inguinale		1
Gonorrhea		1
Chancroid		1

Of the 1,181 patients screened, 141 yielded positive *H. vaginalis* cultures, giving an over-all incidence of 12 per cent. There were 77 cases in the 579 gynecologic patients (13.3 per cent), and 64 cases in the 602 obstetric patients (10.6 per cent). Since "vaginal discharge" was the symptom which prompted many of the nonpregnant patients to be examined, the slightly higher incidence in this group is not considered significant. *H. vaginalis* was not detected in any of the 78 control patients considered to have normal vaginal secretions, nor was the organism isolated from any of the miscellaneous control group, composed of 43 patients (Table IV.)

Reference to Table III shows that 60 per cent of the cases of *H. vaginalis* vaginitis yielded on one or more occasions a pure bacterial culture of the organism.

Of the 1,181 patients studied, 80 (6.8 per cent) had smears positive for trichomonads, but 9 of these had no clinical evidence of trichomoniasis and showed a Grade I bacterial flora. Of the 80 with positive Trichomonas smears, 61 were studied bacteriologically and of these *H. vaginalis* was the predominant bacterial organism in 12 cases (19.7 per cent).

Seventy-nine cases of clinical moniliasis were found in the 1,181 patients, an incidence of 6.7 per cent. Not included were cases which followed antibiotic therapy or patients with incidental positive smears and cultures but without clinical signs and symptoms of moniliasis. Of these 79 patients with a primary diagnosis of moniliasis, 47 were studied bacteriologically and *H. vaginalis* was found to be the predominant organism in two. An additional 5 patients with a primary diagnosis of *H. vaginalis* vaginitis yielded positive cultures of a pathogenic fungus but none of these showed clinical moniliasis.

Only 11 cases could be assigned to the miscellaneous group of bacterial vaginitides, and only three of these showed a Grade III flora, while eight were associated with lactobacilli or diphtheroids. Although evidence of vaginitis was present, the group showed no uniform clinical pattern, diagnosis being more dependent upon bacteriological findings than upon clinical signs.

TABLE IV. ANALYSIS OF ALL PATIENTS STUDIED BY BACTERIOLOGICAL METHODS

		TOTAL NUMBER		
GROUPS	PRIMARY DIAGNOSIS	CASES	POSITIVE FOR H. VAGINALIS	PER CENT OF CASES POSITIVE
1	Bacterial vaginitis	138	127	92.0
2	Trichomonas vaginalis*	61	12	19.7
3	Clinical moniliasis	47	2	4.3
4	Gonorrhea	1	0	0
	Chancroid	1	0	0
	Granuloma inguinale	1	0	0
5	Controls			
	Normals	78	0	0
	Others†	43	0	0
Total		370	141	

\*Including 9 cases without symptoms of trichomoniasis.

†Including cases with excessive amounts of normal-type secretions and with no evidence of vaginal abnormality; cases of cervicitis; cystitis; patients with bloody discharge, etc.

## Pathogenicity

Haemophilus vaginalis is being considered the etiological agent of a specific disease entity and not a component of an abnormal flora resulting from a temporary imbalance in vaginal physiology.

Unequivocal proof of pathogenicity of an organism is dependent on both clinical and laboratory evidence. Four experimental steps, universally known as Koch's postulates, if properly carried out, offer sufficient evidence to define a bacterium as an etiological agent.

Since the bacterium in question is of low virulence, free of serious local manifestations and with no general manifestations, and since the vagina is the site of infection, clinical and bacteriological experimentation could be carried out both safely and conveniently. The steps carried out to establish the organism as a specific etiological agent are described as follows:

#### Koch's Postulates.—

Koch's first postulate: "The bacterium must be observed in every case of the disease." It has been shown (Table IV) that 92 per cent of patients with a primary diagnosis of bacterial vaginitis were found to have H. vaginalis infections.

Kochs second postulate: "The bacterium must be isolated and grown in pure culture." This was accomplished in each of the 141 cases with positive H. vaginalis cultures. Vaginal material from 85 patients yielded H. vaginalis as the only bacterium on one or more occasions, while it was the predominant bacterium in the remaining 56 cases.

Koch's third postulate: "The bacterium, in pure culture, must, when inoculated into a susceptible animal, give rise to the disease." Thirteen volunteer clinic patients, known to be free of the disease, were inoculated with pure cultures of H. vaginalis. Ten of these patients failed to develop clinical evidence of the disease or postive cultures. Two patients yielded positive cultures for two and three months, respectively, but neither developed typical signs of the disease.

One patient developed clinical manifestations of the disease and the organism was recovered in pure culture, having completely replaced the Grade I flora previously present.

That the disease was successfully established from culture material in only one patient did not come as a total surprise. The organism is extremely fastidious, being easily lost even in serial passage. These inoculations were made from culture media which support its growth for only a few days. While work on growth requirements is in progress, the optimal medium has not been determined.

Koch's fourth postulate: "The bacterium must be observed in, and recovered from, the experimentally diseased animal." This requirement was fulfilled, since pure cultures of the bacterium were obtained from the patient successfully inoculated from culture material.

# Other Evidence of Pathogenicity

Not only have Koch's postulates been satisfactorily fulfilled, but other evidence strengthens the case against the organism:

Establishment of the disease in patients (volunteer clinic) inoculated directly (Table V): Fifteen patients proved free of H. vaginalis infection, as indicated by absence of clinical signs and laboratory findings, were inoculated directly with material from the vaginas of infected patients. All donors had been previously tested serologically for syphilis, and by smears and cultures for gonorrhea. Only those donors who showed the typical clinical manifestations of the disease were used and all but one of the donors yielded pure cultures of the organism on the day of the transfer. Weekly cultures were done for five or more weeks after inoculation. As shown in Table V, 11 of the 15 patients inoculated directly developed typical clinical manifestations of the disease. Wet mounts and stained smears showed the characteristic microscopic findings. H. vaginalis was recovered by culture in every inoculated patient who developed clinical signs of the disease. All patients were repeatedly cultured, and each of the 11 "takes" yielded only H. vaginalis on one or more occasions. Since no other pathogenic organisms were present in the donor material, the fulfillment of Koch's third postulate was strongly supported. Some of these patients were allowed to go untreated for as long as four months, and none showed spontaneous cure or alteration in the clinical picture. In two of the successful inoculations the donor material had been taken from patients in whom the disease had been experimentally produced, and these two donors are included in the 11 "takes."

The incubation period can be considered less than seven days, since 8 of the 11 showed clinical signs and positive cultures one week after inoculation.

Husbands of patients with recurrences positive for H. vaginalis: Nine patients developed recurrences of the disease after apparent cures (see criteria under Treatment). Recurrences in apparently cured patients cast suspicion on husbands and it was this which prompted their investigation. Some of the patients who developed recurrences had been free of the disease for as long as six months. Of 41 patients considered cured and followed sufficiently long for making the determination, 9 (22 per cent) developed recurrences. This is a

high figure if one considers the relatively few who were re-exposed during the study. Many of the husbands continued to use condoms, many patients were not exposed because of the stage of pregnancy and puerperium, and several of the husbands were simultaneously treated and cured. Six husbands of the 9 patients with recurrences were studied bacteriologically, and each showed a positive culture for *H. vaginalis*. Eight of the 9 patients with recurrences admitted intercourse without condoms.

TABLE V. RESULTS OF DIRECT INOCULATIONS

CASE	PHYSIOL.	CONSISTENCY		on	ODOR		н	GRADE FLORA	BACT. AFTER	
NO.	STATUS	BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER	BEFORE	INOC.	RESULTS
1	Not preg.	Curdy	Homo.	0 .	XX	4.5	5.2	II	H.V.	Take
2 3	Preg.	Curdy	Homo.	x	XX	4.7	5.2	I	H.V.	Take
3	Preg.	Curdy	Homo.	0	0x	4.7	4.7	I	Dip.	Failure
4	Post- partum	Bloody	Homo.	0	x	4.7	5.0	I	H.V.	Take
5	Post partum	Curdy	Homo.	0	x	5.2	5.5	I	H.V.	Take
6	Preg.	Curdy	Curdy	0	0x	4.7	4.5	I	Lacto.	Failure
7	Preg.	Curdy	Curdy	0	0	4.2	4.2	I	Lacto. Mon.	Failure
8	Postmeno- pausal	Homo.	Homo.	x	xx	5.5	6.6	1	H.V.	Take
9	Post- partum	Curdy	Homo.	x	x	5.5	5.5	II	Lacto.	Failure
10	Not preg.	Curdy	Homo.	0	XX	4.5	5.2	II	H.V.	Take
11	Post- partum	Curdy	Homo.	0	x	4.7	5.0	1	H.V.	Take
12	Post- partum	Homo.	Homo.	0	x	6.8	6.5	II	H.V.	Take
13	Postmeno- pausal	Homo.	Homo.	x	x	7.0	7.2	III	H.V.	Take
14	Not preg.	Curdy	Homo.	0	xx	5.0	5.5	II	H.V.	Take
15	Post- partum	Curdy	Homo.	0	x	4.7	5.5	I	H.V.	Take

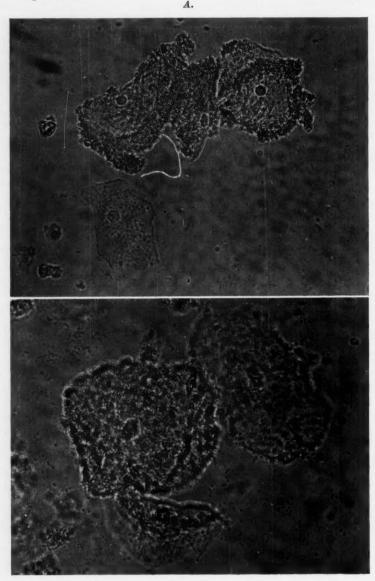
Recovery of H. vaginalis from the urethras of husbands: Cultures were taken by sterile swab from the urethras of 47 husbands whose wives had the disease and the organism was recovered in mixed or pure culture from 45. Of 30 husbands followed by posttreatment cultures, 29 were freed of the organism by one of the three tetracycline antibiotics (Terramycin, Aureomycin, Achromycin) given orally. Several husbands who continued to use condoms and whose wives had remained free of the disease for as long as six months showed positive cultures when finally studied. This observation tends to prove that the organism was more or less permanently established in the urethras of the husbands rather than being present from mechanical deposition. Three husbands developed positive cultures after the disease had been experimentally produced in their wives.

Controls negative for H. vaginalis: Twenty male medical students were studied bacteriologically without a single positive culture being obtained.

Development of the disease in patients immediately following marriage: Two patients, at the time of premarital examinations, were found to have normal floras and no clinical evidence of H. vaginalis vaginitis. Within a few days after marriage, each noticed an odorous discharge. Examinations revealed typical findings of the disease and a pure culture of H. vaginalis was obtained from each. While one husband would not submit to examination, the second yielded a positive culture.

## Diagnosis

The presence of *H. vaginalis* should always be suggested by a gray, homogeneous, and odorous discharge having a pH of 5.0 to 5.5. Although cultural methods are probably necessary to establish final proof of the infection, a careful correlation between clinical signs and microscopic findings offers convincing evidence of its presence.



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Fig. 1.—A, Wet mount showing involvement of epithelial cells with H. vaginalis, referred to as "clue cells." Uninvolved epithelial cell is seen in lower part of field.

B, Higher magnification of epithelial "clue cells."

Wet-Mount Findings.—During the progress of this study, we learned to place great reliance on the appearance of wet mounts. The presence or absence of trichomonads was easily determined, but finding them did not exclude the possibility of an associated H. vaginalis infection (Table III). Leukocytes

usually were not a prominent finding and there was a conspicuous absence of lactobacilli. The appearance of epithelial cells in the wet mount provided the most valuable clue to the presence of H. vaginalis (Fig. 1). There appeared to be varying degrees of disintegration with many of the cells showing indefinite outlines. The cytoplasm showed an especially characteristic granular appearance. This characteristic is due to H. vaginalis being uniformly spaced upon the surface of the cells. Not all cells are involved and some of the affected cells

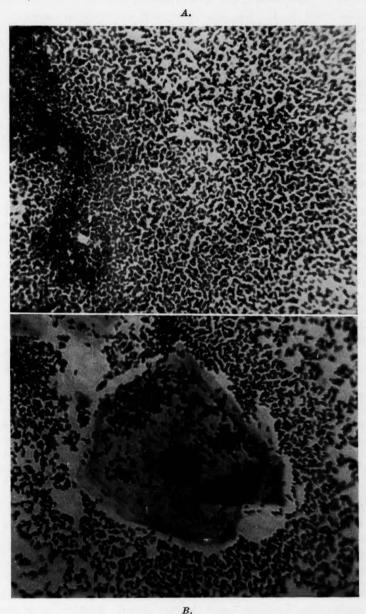


Fig. 2.—Direct smears of vaginal discharge. Note large number of H. vaginalis.

show only partial involvement. For purposes of brevity these finely granulated epithelial cells were frequently referred to as "clue cells." A correct diagnosis could be made in practically every instance on the basis of the wet-mount finding alone.

Stained-Smear Findings.—The most striking feature of the Gram stain is the tremendous number of small gram-negative pleomorphic bacilli frequently forming solid fields outside the cellular elements (Fig. 2).

Culture Findings.—The sheep blood agar plates incubated in a candle jar and the thioglycollate broth were found to be the most reliable media for the initial isolation of H. vaginalis. In the great majority of cases, the sheep blood agar plates were found to contain thousands of minute pin-point colonies after 48 hours' incubation at 37° C. By direct and transmitted light, the surface of the plates frequently appeared to be devoid of bacterial growth. When oblique lighting was employed, however, the myriad of minute colonies could be detected by reflection. Smears taken from these colonies and stained by Gram's method revealed pleomorphic gram-negative bacilli. Subcultures required relatively large inocula (i.e., approximately one hundred colonies), and mixed cultures often presented a difficult problem in the final identification of individual strains.

When the inoculum was small or when the number of organisms present was relatively small, the thioglycollate broth was frequently found to be the most efficient medium for initial isolation. The characteristic "puff-ball" growth of *H. vaginalis* became evident in 48 to 72 hours, and individual "puff-balls" could be subcultured to sheep blood agar plates by means of capillary pipettes.

The completed diagnosis of *H. vaginalis* vaginitis rested upon typical morphology of the colonies and of the organism, typical growth characteristics in thioglycollate broth, and biochemical activity consistent with the pattern described below.

Haemophilus vaginalis is a gram-negative, nonmotile, pleomorphic rod measuring 0.3-0.5 micron wide and 1.0-3.0 microns long. As yet capsules have not been demonstrated. On solid media, growth appears in 24 to 48 hours as minute, pin-point, colorless, transparent colonies 0.05 to 0.2 mm. in diameter, which are most often visible only by reflection from oblique light. Hemolysis is a variable characteristic but when present is a definite aid to the detection of the presence of the colonies. On solid media the organism remains viable from 48 to 72 hours at 37° C., and successful subculture requires a relatively heavy inoculum.

Haemophilus vaginalis has been isolated readily on only one solid medium, Bacto proteose No. 3 agar containing 10 per cent defibrinated sheep blood. Citrated human blood (blood bank) is not a successful substitute for sheep blood. No other solid medium tested to date has been found regularly to support the growth of this organism. Primary isolation is regularly more successful and subsequent growth is stimulated when the cultures are incubated in a candle jar.

In thioglycollate broth, the organism appears to be microaerophilic and growth is inhibited by either methylene blue or resazurin, when these are utilized as eH indicators. Growth in thioglycollate broth is characteristically composed of small (1-2 mm. in diameter) "puff-ball" aggregations dispersed through the upper to middle third of the fluid column appearing after 48 to 72 hours' incubation. Such cultures will remain viable for three to five days at 20° C.

The organism is oxidase negative and produces acid from glucose, maltose, arabinose, rhamnose, levulose, and xylose when cystine trypticase agar is utilized as the fermentation base medium; there is no action on lactose, sucrose, mannitol, trehalose, glycerol, raffinose, salicin, or dulcitol. By the disk method this organism is sensitive to bacitracin, chlortetracycline (Aureomycin), oxytetracycline (Terramycin), tetracycline (Achromycin), usually resistant to chloramphenicol, and is resistant to penicillin, polymyxin, and streptomycin.

#### Treatment

The keenest clinician cannot always differentiate between disordered physiologic states, associated with abnormal floras, and true bacterial vaginitis. It has been suggested that "nonspecific" vaginitis will usually undergo spontaneous cure if factors which disturb normal physiology, such as cervicitis and hypoovarianism, are removed. It is agreed that the majority of bacterial vaginitides or abnormal floras, as the case may be, will undergo spontaneous cure or revert to normal floras with physiological improvement of the patient. It is a routine observation to see Grade II and III floras in postpartum, preadolescent, and postmenopausal patients change to a Grade I flora after natural or artificial elevation of the estrogen level.

Several patients with *H. vaginalis* infections, but without other pathology, showed no improvement while observed for periods as long as six months. Cervical pathology was no more frequent in the infected group than in the control groups. Urinary infections were associated with *H. vaginalis* only three times, and in each of these the urinary infection was caused by a different organism.

Hypoovarianism probably has little relation to H. vaginalis infections. No case of the infection was detected before puberty, and only two cases were found in postmenopausal patients. Hyperestrinism of pregnancy failed to protect patients against either natural contacts or inoculation.

Before the advent of antibiotics and sulfonamides, the treatment of bacterial vaginitis was discouraging because eradication of the causative organism was difficult and recurrences were common. *H. vaginalis* organisms isolated from 41 individual patients were tested against various antibiotics by the disk method. The organism was found to be sensitive to bacitracin and the tetracycline group, usually resistant to chloramphenical and resistant to penicillin, polymyxin, and streptomycin. In view of these sensitivities the tetracycline group was used for treating the majority of the cases, especially in the early part of the study. Triple sulfonamide cream (Ortho) was used as the chief method during the latter part of the present series.

Husbands were instructed to use condoms during treatment and for prolonged posttreatment periods, and all patients were instructed to abstain from douches. The initial follow-up examination was made usually 10 or more days after completion of therapy and 5 or more days after abstinence from intercourse. No case was included in the analysis which was not followed for 30 or more days after completion of therapy, and which had fewer than two post-treatment bacteriological studies.

Of the 60 patients who met these requirements, 48 were considered cured, while 12 were considered treatment failures (Table VI). It is noted that of the 27 patients treated with vaginal Terramycin or Aureomycin, only one treatment failure occurred.

Three patients were treated with procaine penicillin injections, none of whom showed alteration in the clinical or bacteriological picture.

While several treatment failures occurred with the oral tetracyclines, the failures were probably the fault of dosage rather than of the antibiotic.

After treatment with the tetracyclines, secondary infections with Monilia, Proteus, or staphylococci were found to be a frequent aftermath. These infections occasionally constituted a more serious problem than the primary infection. Seeking a method of treatment without this sequela, resort was made to intravaginal triple sulfonamide (Ortho) cream. The cream was injected twice daily for ten days. Of the 13 cases treated by this method, there were 10 cures and 3 failures. Triple sulfonamide cream, it appears, has one advantage over antibiotics in that secondary infections are not encouraged.

Of 41 patients followed sufficiently for the determination, 9 developed recurrences from three weeks to six months after a cure had been ascertained. Six of the husbands of these patients were tested and a positive culture was obtained from each. It may also be recalled that of the 47 husbands of infected wives who were tested, 45 yielded positive cultures. These findings indicate that *H. vaginalis* vaginitis, while being easy to cure, can be expected to recur if husbands are not treated simultaneously.

Table VI. Treatment Methods and Results in 60 Cases of H. vaginalis Infection Followed by Clinical Observations and Cultures for 30 or More Days

After Completion of Treatment

NO. OF				DAYS	RESULTS	
CASES	DRUG	ROUTE	DOSAGE	TREATED	CURED	FAILED
23	Terramycin Suppositories	Vaginal	100 mg. q. 24 hr.	10	22	1
6	Terramycin	Oral	250 mg. q. 8 hr.	5	6	0
6	Achromycin	Oral	250 mg. q. 6 hr.	3	3	3
4	Aureomycin Suppositories	Vaginal	100 mg. q. 24 hr.	10	4	0
2	Aureomycin	Oral	250 mg. q. 6 hr.	4	2	0
2	Aureomycin	Oral	250 mg. q. 8 hr.	2	1	1
1	Aureomycin	Oral	250 mg. q. 12 hr.	2	0	1
1	Procaine penicillin	I.M.	300,000 U. q. 24 hr.	1	0	1
1	Procaine penicillin	I.M.	300,000 U. q. 24 hr.	2	0	1
1	Procaine penicillin	I.M.	600,000 U. q. 24 hr.	2	0	1
13	Triple Sulfa Cream (Ortho)	Vaginal	q. 12 hr.	10	10	3
60	Total		****		48	12

## Comment

To classify all vaginitides without obvious etiology as "nonspecific" has become increasingly unacceptable, and especially so in view of modern bacteriological knowledge. That a regularly appearing predominant organism has not been previously isolated, identified, and associated with so-called "nonspecific" vaginitis is undoubtedly explained on the basis of bacteriological methods in use. Culture media, standardized according to past experience and routinely employed for diagnostic purposes, do not support the growth of the specific etiological agent, H. vaginalis.

After several clinically identical cases of bacterial vaginitis had been studied, and with *H. vaginalis* the only organism isolated consistently, it became clear that a distinct clinical entity had been revealed. Compilation of clinical signs and symptoms showed a definitive pattern for the disease with remarkably few variations. We are convinced that after the findings herein described are confirmed by other investigators, there will be acceptance of the evidence that the majority of so-called "nonspecific" vaginitides are in reality caused by *H. vaginalis*. The supposition that a large group of unrelated bacteria is capable of evoking an identical vaginal syndrome will also have become obsolete. This supposition is undoubtedly explained, in part, by results obtained from culturing the vaginas of women who have not abstained from douching and intercourse. A few colonies of perhaps several species of bacteria cultured from the vaginas of such women should not necessarily be assigned a causative relationship to abnormal discharges, but probably more correctly

should be considered contaminants from the vulva, penis, and douche apparatus. A highly significant observation was the rarity of vaginitis which could be attributed to bacteria other than *H. vaginalis*.

Although *H. vaginalis* was found in only 12 per cent of the present series of 1,181 patients, there is good evidence that the true incidence was considerably higher. A number of patients displaying characteristic clinical and microscopic signs failed to return for cultural confirmation and consequently are not included in the proved incidence. In view of present knowledge, it must be assumed that the majority of these had *H. vaginalis* vaginitis. Many cases undoubtedly escaped clinical detection because of the common practice of pre-examination douching. It has been learned that douching does not eliminate the epithelial "clue cells" of *H. vaginalis*, but wet-mount examination was not used as a screening procedure during the present series.

Although the incidence of *H. vaginalis* vaginitis appeared to be greater than of trichomoniasis, it is not implied that it is a more important clinical entity. While the disease is not a serious one, it is physically and esthetically objectionable, and has undoubtedly contributed to the popular belief that all vaginas are tainted and in need of frequent douching.

Therapeutically, the disease constituted no difficult problem, but regardless of the therapy used it has been demonstrated that husbands must be treated simultaneously if recurrences by reinfection are to be prevented. It has been shown conclusively that the organism is harbored by the male and that he is capable of transmitting the disease by sexual intercourse. Although no careful clinical study was made of husbands, it was observed that, if symptoms were present, they were minimal. Husbands of three experimentally infected women were studied and each developed positive cultures, which demonstrates that a woman can also transmit the organism to her sexual partner. Whether or not the organism resides only in the genital tract and is transmitted only by sexual contact has not been established; therefore, to classify the infection as a venereal disease would be premature.

Apparently *H. vaginalis* is a surface parasite without invasive tendencies. Gross inflammation was an infrequent finding, and histological examination of full-thickness vaginal biopsies from 4 infected patients showed no penetration of the epithelium by bacteria nor evidence of inflammatory reaction.

We await investigation of these findings, recognizing that complete acceptance of *H. vaginalis* vaginitis as a specific entity is pursuant to confirmations. If the results of others are in agreement, it would then appear that the term "nonspecific" bacterial vaginitis should be discouraged or possibly reserved for a small group of cases without definitive patterns and characterized by transient clinical and laboratory findings.

## Summary

Eleven hundred eighty-one patients have been screened clinically for infections of the vagina and 370 were subjected to 1,033 detailed clinical observations and bacteriological studies. One hundred thirty-eight cases with

primary diagnoses of bacterial vaginitis were detected, of which 127 (92.0 per cent) were attributed to a single etiological agent. This bacterium, heretofore unclassified, has been described and assigned the name Haemophilus vaginalis. Proof of pathogenicity of the organism has been presented.

The clinical manifestations of the newly defined vaginitis have been described and criteria for clinical, microscopic, and bacteriological diagnoses given. Special attention has been directed to the diagnostic character of certain epithelial cells designated "clue cells." The results of treatment by several methods are discussed and the necessity of simultaneous treatment of husbands stressed.

Addendum.—Since the completion of this report, a paper by Leopoldo describing a similar organism, isolated from urines of male patients and the cervices of women, has come to our attention.

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## **BREECH PRESENTATION\***

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THE relatively high fetal mortality in breech presentation, so consistently reported by everyone, has not, as yet, been fully explained. Analysis of our own experience will add little, but, in the thought that this little might be helpful, we are herewith presenting our data.

Gordon,<sup>2</sup> Danforth,<sup>1</sup> Morton,<sup>4</sup> Potter,<sup>8</sup> Seeley,<sup>10</sup> and many others have pointed out the high mortality of premature deliveries with breech presentation, and have indicated a higher incidence of breech presentation in premature deliveries. Several writers have suggested that the etiology of breech presentation is, at least in part, due to developmental anomalies in the genital tract; and that, therefore, the physiology of that genital tract is thereby impaired. Numerous writers have also pointed out that major complications of pregnancy, which in themselves bring about premature delivery, would necessarily bring about that delivery at a time when the higher frequency of breech presentation was still present, as compared to delivery at term when many of these breeches would have spontaneously been converted to cephalic presentations.

Relatively few authors have analyzed the presentation relative to the time of death, as related to labor. We have tried to take all of these features into account, but find that our total number of breech presentations (702) does not allow of as satisfactory an analysis as we would like. Particularly discomforting is the fact that we do not have a certain cause of death accurately determined in 18 of our cases where the baby was alive at the onset of labor. Whereas these 18 fetal deaths represent only some 2.5 per cent of the 702 patients, it will be noted that they comprise a rather large proportion (23 per cent) of the deaths (77) in this series. Autopsies were performed on most of these fetuses.

This present analysis has taught us that more careful cooperation between the Departments of Pediatrics, Pathology, and Obstetrics is necessary if we are to improve our performance in the future. We are, just recently, engaged in a so-called perinatal conference on every stillbirth and every neonatal death, regardless of the size of the fetus, with the result that there will be many fewer "unknown" causes of death in the future.

## Incidence

Seeley,<sup>10</sup> Mohler,<sup>3</sup> and Dieckmann<sup>9</sup> all report incidences in excess of 4 per cent. Morton,<sup>4</sup> Danforth,<sup>1</sup> and Potter<sup>8</sup> report incidences between 3 and

<sup>\*</sup>Presented at the Twenty-second Annual Meeting of the Central Association of Obstetricians and Gynecologists, St. Louis, Mo., Oct. 7 to 9, 1954.

4 per cent. In our own clinic, in the earlier years when many patients were referred because of a known breech presentation, our incidence was 5.1 per cent. More recently, when a much higher percentage of our patients have been "registered" cases, the incidence has decreased to 3.8 per cent. It seems probable that the correct incidence the country over is greater than 3 per cent but, perhaps, less than 4 per cent. Distributionally, the incidence is quite well shown in Table I. The relatively very high incidence of breech presentation in the smaller weight groups would naturally account for a considerable number of breech deaths on the basis of immaturity and prematurity alone. That this explanation is not entirely adequate is obvious from the inspection of Table II, which shows a consistently higher mortality for breech as compared to cephalic presentation regardless of weight group. A particularly striking difference is to be noted in the babies of 4,000 grams and over, where with cephalic presentation the mortality is 3 per cent as compared to 23 per cent for breech presentation. This high mortality with large babies has been previously reported by Danforth, Gordon, and Seeley. Perhaps some of these very large breech babies should be delivered by section.

TABLE I. DISTRIBUTIONAL INCIDENCE

	TOTAL NUMBER	BREECH	PER CENT
500- 995 grams	46	16	34.8
1,000-1,495 grams	171	39	22.8
1,500-2,495 grams	1,348	205	15.2
2,500-3,995 grams	13,284	416	3.1
4,000 grams and over	913	26	2.8

TABLE II. DISTRIBUTIONAL MORTALITY

	CEPHALIC	BREECH
500- 995 grams	75 %	94 %
1,000-1,495 grams	56 %	64 %
1,500-2,495 grams	11.5%	22.4%
2,500-3,995 grams	1.2%	5.0%
4,000 grams and over	3.1%	23 %

## Type of Labor

There has been the intimation that breech presentation tended to result in a somewhat abnormal labor. Not much has been said about this one way or another in the literature. We have previously reported that breech presentation would not result in prolonged or difficult first stage labor. It has been our impression that the second stage of labor was a little more difficult, due to the markedly altered mechanism of labor; and personal conversations with our experienced friends-Litzenberg, McCord, Kimbrough, and othershave corroborated this impression. We find that there is no difference in the first stage of labor (Table III) in our experience. The second stage of labor seems to be somewhat longer in multiparas, and the third stage of labor seems to be associated with somewhat larger blood loss in multiparas. Whether these minor differences are the result of our mismanagement or actually inherent in the breech presentation itself is definitely open to question. The fact that there seems to be no difference between cephalic and breech presentation in primiparas in respect to either the duration of the first stage of labor, the duration of the second stage of labor, or the blood loss in the third stage of labor seems to be significant. It is also interesting at this point to note that in the last several years we have had no fetal mortality in primiparous patients which has been ascribed to the breech presentation.

TABLE III. DURATION OF LABOR

	CEPI	HALIC	BREECH		
	PRIMIPARAS	MULTIPARAS	PRIMIPARAS	MULTIPARAS	
Duration first stage (hours)	13.9	7.9	12.6	7.9	
Duration second stage (minutes)	44	11	44	26	
Third stage blood loss (c.c.)	210	172	207	225	

# Major Complications of Pregnancy

Having previously noted a peculiarly high incidence of fetal death due to congenital anomalies inconsistent with extrauterine life (9 deaths in the 702 patients, or 1.3 per cent), as compared to a much lower rate with cephalic presentations (31 in 14,401 or 0.2 per cent), we have tried to analyze the effect of major complications of pregnancy in the same way, and find very much the same results. Taking into consideration only those cases in which the fetus is alive at the onset of labor, we had 17 deaths in the breech patients, or 2.4 per cent, as compared to 78 deaths in the cephalic presentations, or 0.5 per cent. One can, of course, immediately raise the question whether these deaths were entirely due to the major complications or whether, in a good many instances, they may have been due to the method of management of that complication. The latter appears to have been true in the days when labor was induced in toxemia and placenta previa patients by the use of the Voorhees' bag. The virtual abandonment of combined podalic version in the treatment of placenta previa, with the resultant improvement, seems further to corroborate this idea.

TABLE IV. CESAREAN SECTION IN BREECH VS. CEPHALIC PRESENTATION

	TOXI	EMIA.	PREMATURE SEPARATION		PLACENTA PREVIA		DIABETES	
WEIGHT OF FETUS (GRAMS)	CE- PHALIC	BREECH	CE- PHALIC	BREECH	CE- PHALIC	BREECH	CE- PHALIC	BREECH
500- 995	0	0	0	0	0	0	0	0
1,000-1,495	4 (2)	1 (1)	1	2 (1)	3	0	0	0
1,500*-2,495	20 (1)	4	6 (1)	4 (1)	10 (3)	3 (1)	1 (1)	0
2,500-3,995	21 (2)	3	3 (1)	1	15	2	10 (3)	0
4,000 and over	2 (1)	0	0 .	0	. 0	0	1 `	0

\*All sections in cases where the fetus weighed under 1,500 grams were done for maternal reasons.

†Numbers in parentheses represent fetal deaths in cases where the fetus was alive at the onset of labor.

Since cesarean section has been more frequently used in the treatment of these major complications of pregnancy, it also seemed wise to note whether its use had had any particular effect upon the mortality rate under these circumstances. Table IV shows the relative results with breech and cephalic presentation when section was done for the various major complications at the various weight levels. In the breech patients, 2 babies of 1,000 grams each were lost due to unknown cause. One was lost because of congenital anomaly and one because of hyaline membrane. In the cephalic presentations, 3 were lost from unknown causes, 3 from hyaline membrane, 3 from congenital anomalies. Two were lost due to the toxemia (because the cesarean was too long delayed?). Two were lost from trauma because the section was not done until the patient had already been in labor more than thirty hours with a firm cervix, and 2 were dead before a section was done because of a Couvelaire uterus. Table V shows the comparable figures for vaginal delivery. When

one considers that the cesarean sections were done in the much less favorable cases, the contrast is quite striking, and strongly suggests that cesarean section might well be preferable in certain patients with major complications of pregnancy, where the fetus weighs between 1,500 and 2,500 grams. In term patients, the breech presentation presents much less of a hazard.

TABLE V. VAGINAL DELIVERY IN BREECH VS. CEPHALIC PRESENTATION

	TOX	EMIA	PREMATURE SEPARATION			ENTA	DIABETES	
WEIGHT OF FETUS (GRAMS)	CE- PHALIC	BREECH	CE- PHALIC	BREECH	CE- PHALIC	BREECH	CE- PHALIC	BREECH
500- 995	3 (1)	* 2	4 (3)	2 (2)	1 (1)	1 (1)	0	0
1,000-1,495	24 (9)	3 (1)	15 (4)	9 (4)	4 (3)	1 (1)	0	0
1,500-2,495	103 (7)	9 (1)	38 (7)	6 (3)	10 (2)	6 (2)	4	2
2,500-3,995	451 (9)	17	63 (5)	5	50 (6)	2	9	0
4,000 and over	32 (3)	2 (1)	1	1 (1)	0	0 .	8 (3)	0

\*Numbers in parentheses represent fetal deaths in cases where the fetus was alive at the onset of labor.

TABLE VI. TWENTY INTRAPARTUM DEATHS

CAUSE	NO.	WEIGHTS (GRAMS)
Congenital anomaly	2	2,770, 4,900
Premature separation of placenta	4	545, 1,810, 1,885, 4,650
Placenta previa	2	1,660, 2,010
Erythroblastosis	1	2,440
Hyaline membrane	1	2,465
Toxemia	1	4,365
	11	
Trauma (including firm cervix and prolonged labor)	4	2,975, 3,350, 3,500, 3,810
Prolapsed cord	3	1,605, 2,210, 3,025
"Unknown"	2	1,960, 2,455
	9	

TABLE VII. FIFTY-SEVEN POSTPARTUM DEATHS

CAUSE	NO.	WEIGHTS (GRAMS)				
Congenital anomaly	7	1,810, 1,900, 2,160, 2,490, 2,695, 2,780, 2,925				
Toxemia	3	1,000, 1,100, 1,590				
Premature separation of placenta	6	600, 1,000, 1,305, 1,310, 1,480, 1,660				
Other placenta	1	1,170				
Placenta previa	2	985, 1,110				
Syphilis	1	1,990				
Pneumonia	3	1,440, 2,580, 3,670				
Other infection	2	1,880, 3,015				
Hyaline membrane	7	1,175, 1,190, 1,550, 1,595, 1,680, 1,775, 1,900				
Erythroblastosis	1	1,800				
	33					
Trauma	7	1,095, 1,310, 1,540, 1,765, 1,880, 3,225, 4,050				
Prolapsed cord	1	1,590				
Unknown	16	680, 750, 800, 820, 855, 920, 920, 980, 990, 990				
		1,000, 1,170, 1,550, 1,560, 2,100, 3,340				
	24	-,, -,, -,, 2,000, 2,200, 0,020				

# Corrected Fetal Mortality

A more detailed analysis of the 20 deaths which occurred during labor and the 57 neonatal deaths, eliminating those deaths due to congenital anomalies, major complications of pregnancy, infection, and erythroblastosis, shows us that the remaining deaths (due to trauma, prolapsed cord, and unknown causes) still leave (Table VI and Table VII) a much higher death rate in breech presentation than in cephalic deliveries. It may not be entirely fair to include the unknown patients in this group. Since, however, only two intrapartum deaths in the breech group were found to be apparently without cause, the discrepancy, if any, cannot be great. Even in the postpartum group, most of the deaths were of infants under 1,500 grams. We should probably again emphasize the hazard of breech presentation of infants that weigh under 1,500 grams. Between 1,500 and 2,500 grams, there is still a considerable differential. Above 2,500 grams, one can have considerable equanimity unless the fetus considerably exceeds 4,000 grams.

# Normal Pregnancy and Labor

In patients with a normal prenatal course, without major complications of pregnancy and eliminating congenital anomalies, hyaline membranes, erythroblastosis, etc., we have a residuum of cases which are analyzed in Table VIII. It will be seen that at whatever fetal age delivery takes place, the mortality in breech presentation is definitely higher than when the baby presents by the occiput. The only value of this table, as we see it, is that it clearly shows that the mortality in breech presentation is not the 10 per cent usually quoted, but that a considerably smaller figure represents the true state of affairs. It is apparently about a 2 per cent factor in full-term babies (2.2 per cent mortality as against 0.3 per cent mortality for occiput presentation).

TABLE VIII. DEATHS DUE TO PROLAPSED CORD, TRAUMA, AND "UNKNOWN" CAUSES, IN "NORMAL" BREECH VS. CEPHALIC PRESENTATION

	1	CEPHALIC	BREECH			
WEIGHT OF FETUS	NO. DEATHS		s*	NO.	DEATHS*	
(GRAMS)	CASES	NO.	%	CASES	NO.	%
500- 995	23	13 (13)†	57	11	9 (9)	82
1,000-1,495	56	7 (6)	13	20	3 (1)	15
1,500-2,495	907	14 (7)	1.5	165	11 (4)	7
2,500-3,995	11,758	34 (11)	0.3	382	8(1)	2.1
4,000 and over	784	10(1)	1.3	21	1	5
Total						
Above 1,000 grams	13,505	65	0.5	588	23	4
Above 1,500 grams	13,449	58	0.4	568	20	3.
Term babies	12,542	44	0.3	403	9	2.5

\*Those fetuses known to be alive at onset of labor.

†Numbers in parentheses represent deaths the cause of which was "unknown."

That this figure is in part dependent upon the method of management of the breech presentation has been clearly pointed out previously by Gordon,<sup>2</sup> Baer,<sup>5</sup> Hanson, and others. We are completely in accord with these authors, and have never favored breech extraction or "breaking up" the breech, preferring to have the babies delivered spontaneously, or by the "assisted breech" technique. The plan advocated by Dr. Robert Kimbrough, of having the mother put the buttocks "in our hand" before assistance is given, particularly appeals to us. Irving Potter and others have clearly demonstrated that there is no need for speed from this point but, rather, that gentleness and skill of manipulation are much more important. An early and deep episiotomy is recommended.

We have always felt that with a borderline pelvis, where we might well recommend a trial of labor with an occiput presentation, such trial labors should probably not be recommended with breech presentations. Until very recently, the exact size of the fetal head has not been readily determined, but with the institution of 14 foot x-ray pictures, head size can now be as well determined with one presentation as with another. The advantage of head molding with cephalic presentation will always make trial of labor less desirable in breech presentations. The advantage of cesarean section, when the breech is combined with major complications of pregnancy, has still to be proved; but present figures seem to indicate that abdominal delivery is to be seriously considered in some of these circumstances.

It goes without saying that one should strictly avoid artificial rupture of the membranes, at least until the baby is ready to be delivered. Prolapse of the cord is, in our experience, not only more frequent with breech presentation but also more lethal. It also seems highly unlikely that incision of the cervix, which is holding back the aftercoming head, will ever accomplish uniformly good results. We have taught that the presence of a skilled assistant, who knows how to guide the aftercoming head into the pelvis is more important in a breech delivery than such an assistant at a cesarean section. We still feel this to be so. The very fact that, in our own patients, the fetal mortality is higher in multiparas than in primiparas has caused us to wonder whether some of our house staff have not become careless about having such an assistant with the multiparous patients.

We do not agree that the application of the Piper forceps should be a routine procedure for the aftercoming head, but that these forceps should always be available on the side table is very important.

#### Summary

Although breech presentation does not lead to an abnormal first, second, or third stage of labor, it is associated with increased fetal mortality for several reasons:

- 1. It is more frequent in immature and premature deliveries, in both of which there is increased fetal loss.
- 2. Major complications of pregnancy are often terminated early before breech presentation is spontaneously converted to cephalic presentation. Increased knowledge of how best to treat these major complications will inevitably lead to a decreased fetal mortality in breech presentation.
- 3. Prolapsed cord and birth trauma are more common and more fatal with breech presentation.
- 4. Even with normal pregnancy and "normal" labor, there is increased danger which can, at least in part, as pointed out by Gordon many years ago, be alleviated by proper management of labor.
- 5. The fetal mortality rate should not be in the range of 10 per cent but more nearly somewhere near 2 per cent.

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#### Discussion

DR. RALPH LUIKART, Omaha, Neb .- Dr. Calkins, in his report of 702 breech presentations, has shown the relationship of fetal mortality rates in breech deliveries to the length of the gestation period and the weight of the baby. Table II shows an incidence of fetal mortality in babies with breech presentation weighing 4,000 grams and over. The fetal mortality is almost five times that of babies in the 2,500 to 3,995 gram weight group. The essayist stated "perhaps some of these large breech babies should be delivered by cesarean." With this statement I heartily agree. Perhaps we should be a little less conservative but how are the large breech babies to be diagnosed in the absence of facilities for getting the 14 foot x-ray mentioned by Dr. Calkins? We do not have facilities for that technique in Omaha.

Dr. Dieckmann and others have advocated an attempt at external version in breeches around the thirty-sixth week of gestation. Dr. Stevenson's study showed that the position of the implantation of the placenta determined the position of the fetus in uetro in a high percentage of pregnancies. The position of the placenta was determined by softtissue x-ray and tenderness of the uterus in the area of the placental sight. Stevenson's findings have convinced me that external version is not practical from a mechanical standpoint. Often the results are only temporary and certainly the procedure is not free from the danger of dislodging the placental atachment. I believe the risk of damage is too great for the possible gain.

Dr. Calkins has referred to the prophylactic care in breech presentation, about which I wish to emphasize the following: unimpeachable prenatal care; intelligent sedation and analgesia such as pudendal block; anesthesia, if used, given by a well-trained anesthesiologist; constant observation of the fetal heart rate; episiotomy if indicated; a deliberate and unhurried delivery; forceps judiciously applied to the aftercoming head with the least possible trauma; and, last but not least, there should be immediately available a doctor, preferably a pediatrician experienced in any methods of resuscitation that might be needed. There should be available proper facilities, including carbon dioxide, oxygen, laryngoscope, and any drugs needed.

(Closing discussion on page 994.)

# END RESULTS OF BREECH DELIVERIES AT LEWIS MEMORIAL MATERNITY HOSPITAL\*†

Based on a Twenty-One-Year Study

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THE management of breech presentation remains a controversial subject. The ultimate answer must come from the critical evaluation of end results with the methods employed. With this in mind, a detailed study was made on all breeches delivered at Lewis Memorial Maternity Hospital from 1930 to 1952. An effort was made to evaluate various intrinsic factors of breech presentation in order to determine their influence on fetal and maternal outcome. The mathematical occurrence of some features certainly must imply a natural effort at compensation for malposition. No effort was made to correlate findings with the theories of etiology<sup>16, 17</sup> of breech presentation and no clinical features were noted which offered any new theory.

#### Incidence

Various authors report from 3 to 4.8 per cent of all presentations as by the breech. Eastman<sup>6</sup> quotes 3.11 to 3.9 per cent; Greenhill<sup>8</sup> from 4 to 4.5 per cent. All large series for the past 10 years were added.<sup>1, 7, 9, 10, 13, 14, 17, 18, 19, 21, 22</sup> A total of 270,847 deliveries yielded 11,391 breech presentations. Combined with our series, this is an incidence of 4.2 per cent. Of the 1,512 mothers delivered at Lewis Memorial Maternity Hospital, 727 were primiparas (48.1 per cent) and 785 multiparas (51.8 per cent). In totaling our numbers with those of other authors, <sup>1, 10, 18, 19, 22</sup> an incidence of 52.6 per cent for primiparas and 48.3 per cent for multiparas was found.

#### Material

This material is obtained from 38,962 deliveries, 1,544 of these being breech presentations in 1,512 mothers. This number includes all breech presentations, regardless of length of gestation, but excludes all version-extractions and cesarean sections.

Type of Breech Presentation.—Eighty-nine per cent of our breech presentations were frank or complete, and 11 per cent were footling. Ware and associates<sup>19</sup> had only 7 per cent footling and Tompkins<sup>17</sup> as high as 33 per cent footling. A summary of various authors' results<sup>1, 17, 19, 22</sup> gives 80 per cent as frank and complete, and 20 per cent as footling.

<sup>\*</sup>This study was in part made possible by a grant from the Henry Schmitz Medical Foundation.

<sup>†</sup>Presented at the Twenty-second Annual Meeting of the Central Association of Obstetricians and Gynecologists, St. Louis, Mo., Oct. 7 to 9, 1954.

Position of Breech.—Eastman<sup>6</sup> states 64 per cent of occipital positions are left, and 36 per cent are right. An effort to determine a corresponding proportion in breech presentations in our series showed 55.4 per cent were left sacrum and 44.6 per cent were right sacrum. Tabulation of various authors' results<sup>1, 3, 11, 15</sup> shows 54.6 per cent to be left sacrum and 45.4 per cent to be right sacrum. Left anterior position occurred four times as often as left posterior, and right anterior position occurred three times as often as right posterior.

#### Results

Maternal Mortality and Morbidity.—Meyer<sup>10</sup> encountered 9.9 per cent maternal morbidity with all vaginal breech deliveries. In our group there were 128 cases of morbidity. This is an incidence of 8.5 per cent. The causes of this morbidity are listed in Table I.

TABLE I. MATERNAL MORBIDITY (TOTAL 128 CASES)

Urethritis and cystitis	46
Pyelitis	38
Thrombophlebitis	8
Infected episiotomies	8
Disrupted episiotomies	6
Upper respiratory infections	6
Eclampsia with convulsions	5
Breast abscess	5
Endometritis	3
Nephrosis	1
Peripheral neuritis	1
Infectious hepatitis	1

Of the mothers in this series, 10.3 per cent of the primiparas were morbid, and 6.9 per cent of the multiparas; 17.2 per cent of 58 primiparas over 30 years of age and 14.6 per cent of 96 multiparas over 30 years had a morbid puerperium. In primiparas over 40 years of age, Walsh and Kuder<sup>18</sup> reported an 18 per cent incidence of morbidity.

The method of delivery affected the morbidity greatly. Spontaneous, aided, and extracted deliveries are compared. We have defined spontaneous delivery as a guided delivery with the fetus delivered only by maternal forces. An aided delivery is a delivery completed by the obstetrician after the fetus is delivered to the scapulas or umbilicus by maternal forces alone. An extraction delivery is a delivery by manual traction on the feet or breech before the fetus presents at the outlet; this type of delivery includes decomposition. Many authors have stated that extraction of a breech carries a higher maternal morbidity and higher infant mortality than spontaneous or aided deliveries. There were 61 morbid patients among 1,143 delivered by spontaneous mechanism or aid, a percentage of 5.3. The remaining 68 morbid cases were distributed among 369 mothers who had extracted deliveries (18.4 per cent). The maternal morbidity and infant mortality and the type of delivery are shown in Fig. 1, compared to Zacharias 22 results for standardization.

The incidence of postpartum hemorrhage is also reflected in the type of delivery. Postpartum hemorrhage occurred after 2.62 per cent of the spontaneous and aided deliveries and after 8.4 per cent of the breech extractions. There were 61 instances of postpartum hemorrhage in our entire group, an incidence of 4.04 per cent; 45 (74 per cent) of these were primiparas and 16 (26 per cent) were multiparas.

There were four deaths of mothers with breech presentations during the 21 years of this study. These deaths were not attributable to the presentation

of the fetus, however. They were caused by: (1) an intestinal obstruction post section; (2) aspiration of emesis at delivery; (3) eclampsia in a patient who refused treatment and entered the hospital in extremis; and (4) a ruptured appendix with death on the third postpartum day. The uncorrected mortality rate is 0.26 per cent; corrected is 0.0.

Length of Labor and Method of Delivery.—All of our cases were surveyed for the length of labor and the type of delivery. Labors for breech deliveries are shorter than labors for other presentations. For all presentations, Eastman<sup>6</sup> gives 17.7 hours for primiparas and 12 hours for multiparas. Primiparas in our series averaged 14.5 hours of labor and multiparas averaged 8.9 hours of labor. Meyer<sup>10</sup> reported averages as high as 17.5 hours for primiparous labors and 11.5 hours for multiparous labors. Ware and co-workers<sup>19</sup> reported an average of 10.5 hours for primiparas and 8.7 hours for multiparas.

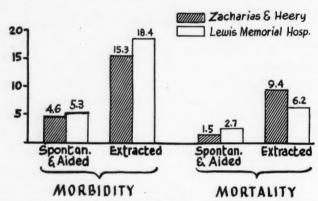


Fig. 1.—Comparison of fetal mortality and maternal morbidity in the different types of breech delivery (spontaneous and aided, and extracted).

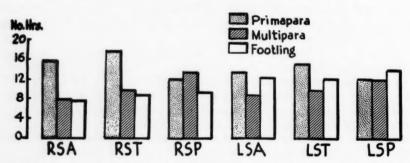


Fig. 2.—Variations in the length of labor in primiparas, multiparas, and in footling presentation, with the various positions of the breech.

It is interesting to note in our series that the longest labors in primiparas were with transverse positions of the breech; multiparas took longer to complete labor in the posterior positions. It took much less time to complete labor with footlings than with frank or full positions; footlings taking longest with posterior positions and left longer than right. These variances are shown in Fig. 2. When all the breeches are compared to footlings as to parity, length of labor and type of delivery, a great difference is apparent.

In studying our prolonged labors, we noted that the position of the fetus had very little effect upon the prolonged labor. Tabulations of the lengths of labor with right and left sacrum positions and anterior, transverse, and posterior positions showed no significant differences.

# Fetal Mortality and Morbidity

For the 1,544 infants delivered in our series, the gross mortality rate was 12.12 per cent. Correcting for prematurity, previability, and developmental abnormalities, the mortality was 4.12 per cent. A comparison of birth weight and the incidence of fetal death is shown in Fig. 3. The infant mortality decreased markedly with every increase of 500 grams in weight until infants weighed over 4,500 grams.

Prolapsed cord occurred 45 times, 34 times in multiparas and 11 times in primiparas. In 43 of these, extraction was done and 4 fetal deaths resulted. This is an 8.9 per cent mortality (over twice our over-all mortality rate). Pomerance and Daichman<sup>12</sup> reported a 25 per cent fetal mortality in cases of prolapsed cord, and Cope<sup>4</sup> stated that in frank breech with prolapsed cord there is only a 57.5 per cent survival rate.

The largest single cause of fetal death in our corrected series was cerebral (hemorrhage and/or edema); these were considered as a group. Twenty of these babies were delivered by extraction; 2 had aided deliveries. Eleven mothers were primiparas and 11 were multiparas. Six deliveries were footlings. Five of the babies weighed over 4,000 grams. Seven premature babies had tears of the tentorium and falx. These infants averaged only 4 pounds in weight. Therefore, the danger of cerebral damage is present in small infants as well as in normal or large infants.

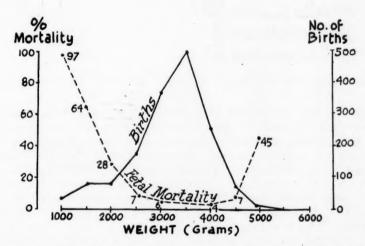


Fig. 3.—Comparison of the percentage of fetal mortality with fetal weight at delivery in 1,544 fetuses.

The large infants present a special problem. Cox<sup>5</sup> reported a 10 per cent fetal mortality in infants over 7½ pounds. In our series, there were 81 infants over 4,000 grams. Ten of these died (12.3 per cent). Maternal postpartum hemorrhages occurred in 11 (all over 1,000 c.c.). There were 16 instances of prolonged labor; of these 16, 8 were in primiparas and 8 in multiparas.

Necropsies were performed on 39 of the 49 (corrected figure) infants that died, and, of these, 22 deaths were caused by cerebral hemorrhage and/or cerebral edema. The causes of all 49 deaths are itemized in Fig. 4.

Thirty-five infants were morbid (2.27 per cent) and 20 of these cases were of traumatic origin. The cause of all 35 cases are listed in Table II.

There were 25 developmental abnormalities, an incidence of 1.6 per cent.

TABLE II. FETAL MORBIDITY (35 CASES)

Traumatic.—		
Fractured clavicle	10	
Fractured humerus	4	
Erb's palsy	1	
Convulsions	4	
Massive scrotal hemorrhage	1	
Adjustment.—		
Atelectasis	6	
Asphyxia	4	
Dyspnea	1	
Erythroblastosis	1	
Infectious.—		
Bronchopneumonia	3	

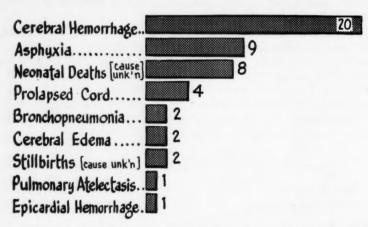


Fig. 4.—Causes of 49 fetal deaths (corrected figure) in 1,544 breech deliveries.

Prolonged Labor and Fetal Mortality.—There were 131 instances of prolonged labor (8.7 per cent of our series), but 21.8 per cent of our corrected number of fetal deaths occurred with prolonged labor. Pomerance and Daichman<sup>12</sup> have shown a direct relation between fetal and neonatal loss with increasing duration of labor, from 2.9 per cent fetal mortality with labor under twelve hours to 19.0 per cent fetal mortality with labor over forty-eight hours. Of our 131 cases of prolonged labor, 12 infants died, giving us a corrected infant mortality of 9.2 per cent. This stayed almost constant for the two periods of time. This is shown in Table III.

TABLE III. PROLONGED LABOR AND FETAL MORTALITY

•	NUMBER PROLONGED	FETAL DEATHS	% MORTALITY
1931-40	88	8	9.1
1941-52	43	4	9.3
1931-52	131	12	9.2

The Influence of Episiotomy on Fetal Mortality and Morbidity.—Many authors, in considering breech delivery, dwell upon the use of and need for an adequate episiotomy for fetal protection. Their opinion is that cerebral damage is decreased greatly by the use of episiotomy. Barney and Bill, in discussing Potter's<sup>13</sup> article, state that episiotomy is a child saver and is obligatory in all breech deliveries. There are no reported statistics upon the efficacy of episiotomy. Our deliveries were reviewed with this in mind. Of

the 1,544 infants delivered, 1,187 were at term and without abnormality. Of these 1,187, 694 were delivered with associated episiotomy. The result of comparing fetal deaths with and without the use of episiotomy is very illuminating. Without the use of episiotomy, over twice the fetal mortality rate is encountered as compared to that with the use of episiotomy. Results are shown in Fig. 5.

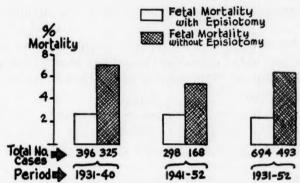


Fig. 5.—The influence of episiotomy on fetal mortality. Comparison of the number of deaths with and without the use of episiotomy.

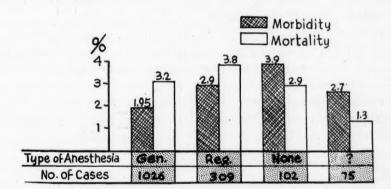


Fig. 6.—The type of anesthesia (general, regional, none, and unknown) and its influence on maternal morbidity and fetal mortality.

The use of forceps on the aftercoming head was studied in relation to fetal mortality. These were applied 256 times, an incidence of 21 per cent; 74 per cent of these applications were in difficult deliveries. In these cases where forceps were applied, there were 11 fetal deaths (4.29 per cent mortality). This fetal mortality approximates our over-all rate of 4.12 per cent.

Anesthesia.—Anesthetics were studied in an effort to determine the effect of general anesthesia, regional anesthesia, and no anesthesia on fetal mortality and morbidity. Fetal morbidity was highest without anesthesia and lowest with general. Fetal mortality was highest with regional anesthesia. These comparisons are shown in Fig. 6.

Nuchal Arms.—These were encountered 34 times in this series (2.2 per cent). Thirty of these were delivered by extraction and in these 6 clavicles and 2 humeri were fractured (26.7 per cent morbidity). One neck was broken. Twenty-two of these mothers were primiparas and 12 were multiparas.

# Summary

- 1. In thirty-one years at Lewis Memorial Maternity Hospital, 38,962 deliveries yielded 1,544 breeches, an incidence of 3.9 per cent.
- 2. Maternal morbidity was 8.5 per cent; corrected maternal mortality was 0.0.
- 3. Breech extraction, as opposed to aided or spontaneous deliveries, cause the highest puerperal morbidity and over twice the number of postpartum hemorrhages.
- 4. Mothers delivered by extraction were in labor 30 per cent longer than with spontaneous and aided deliveries. Footlings were delivered after shorter labors than other breeches. The position of the breech had no effect upon the length of prolonged labors.
- 5. The corrected fetal mortality was 4.12 per cent. The fetal morbidity was 2.27 per cent. The cause of the largest number of fetal deaths was cerebral hemorrhage, and the largest number of cases of fetal morbidity were of traumatic origin.
- 6. Delivery by extraction and prolonged labor both carried a much higher fetal mortality than did spontaneous and aided deliveries.
- 7. The use of episiotomy was associated with less than half the fetal mortality associated with no episiotomy.
- 8. General anesthesia, in contrast to regional or no anesthesia, had the lowest associated fetal morbidity; regional had the highest mortality.
- 9. Nuchal arms were associated with traumatic morbidity in 26.7 per cent of cases.
  - 10. Prolapsed cords caused an 8.9 per cent fetal mortality.
- 11. Higher fetal mortality and more postpartum hemorrhages accompanied delivery of very large infants in breech presentation.

## Conclusions

The results of this study support our present management of breech presentation at Lewis Memorial Maternity Hospital. Our policy is:

- 1. Spontaneous delivery of the breech to the scapulas or umbilicus.
- 2. Deep ether anesthesia.
- 3. Close observation and full supportive measures in all normal and prolonged labors.
  - 4. The use of a large episiotomy in all breech deliveries.
- 5. Forceps on the aftercoming head in all instances where the head does not deliver easily.

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#### Discussion

DR. GEORGE WULFF, JR., St. Louis, Mo.—Breech presentation demands even more attention by the leaders of our specialty. It occurs once in every 25 to 30 deliveries, and carries with it a fetal mortality of over 4 per cent. We must all study in an effort to reduce this high death rate. It is an accepted fact that this mortality rate is several times greater than that associated with cephalic presentations and many authors feel that this differential is sufficient to warrant the use of routine external version in an attempt to prevent breech presentations from delivering as such.

The authors have carefully compared their statistics with those of other authors and in addition have pointed out certain facts which will be of great value to the rest of us when confronted with this presentation. Their figures emphasize that there was a higher fetal mortality associated with breech extractions, prolonged labors, very large babies, conduction anesthetics, and in those cases in which no episiotomy was performed.

It is stated that the greatest cause of fetal death was cerebral hemorrhage, the largest number of cases of fetal morbidity were traumatic, and that forceps on the aftercoming head were efficacious in difficult deliveries. Of the autopsied fetal deaths, 56 per cent were caused by cerebral hemorrhage, and of 35 fetal morbid cases, 57 per cent were caused by trauma.

Breech presentations at St. Louis Maternity Hospital for the sixteen-year period, 1936 through 1951, were reported recently by Dr. A. C. Trueblood and myself. In this series there were 44 corrected fetal deaths out of 1,040 breech cases, a fetal mortality of 4.23 per cent, which is almost identical with the authors' figure of 4.12 per cent. Of our 34 autopsied cases, 19, or 56 per cent, were caused by cerebral hemorrhage—this figure is identical with that of today's paper.

If the greatest single cause of fetal death in breech presentation can therefore be assumed to be intracranial damage, then it seems to follow that primary efforts to reduce this mortality must be directed at the prevention of damage to the aftercoming head itself. Although forceps have long been recognized as a possible method of delivery of the aftercoming head, they have almost universally been utilized as a second choice to the spontaneous method. It is our earnest feeling that the procedure of choice in managing the aftercoming head should be reversed, and that the protection of the aftercoming head by elective, primary use of forceps will definitely reduce the dangers to the fetus from intracranial trauma and hemorrhage. The purpose of the forceps should be twofold; first, to protect the head from compression from outside forces, both those in the birth canal, and those of an overanxious assistant; and, second, to allow the head to be moved through the pelvis and over the perineum with great care and a deliberate lack of haste. This latter point has only in recent years been sufficiently emphasized. For many years, students have been impressed with the need for hasty delivery of a breech baby as soon as the umbilicus was delivered, and the methods of forceful expulsion of the aftercoming head were designed in an effort to hasten this entire process. Potter, we know, was very instrumental in showing the fallacy in this need for haste, and other authors in recent years have pointed out that deliberate care is considerably more important than rapidity in the management of these cases. Schwarz said, "Pressure from above, if exerted with full force by an assistant, undeniably may become directly responsible for severe intracranial hemorrhage." Routine early and primary use of the forceps offers an excellent solution to this problem. Since the operator requires both his hands free for the forceps application, his assistant must support the baby by the feet and arms. With both hands so well occupied, no assistant will be able to make traumatizing fundal pressure.

I strongly urge that we, as the leaders in our specialty, say, "Our policy is [to use] forceps on the aftercoming head!"

DR. HAROLD S. MORGAN, Lincoln, Neb.—I wish to call attention to the fact that in 1940 a member of this Association, the late Elmer Hansen, presented a series of 136 cases of breech presentation, with a fetal mortality of 0.8 per cent.

Our group operating at Lincoln General Hospital, Lincoln, has followed the five concepts recorded by Hansen in 1940 and published in the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY.

Our experience with the management of breech presentation, along the conservative lines advocated by Hansen, originally, and repeated by Calkins' and Schmitz' papers this morning, gave a corrected fetal mortality of 1 per cent. I suspect if we had corrected along the same line that Dr. Calkins did we would have a slightly higher fetal mortality than 1 per cent, but I believe that fetal mortality in breech, associated with a conservative management, should never go above 2 per cent, and, as I pointed out, we have a series of 500 cases with 1 per cent. In this entire series of 500 cases, external version was never attempted and never done.

This low mortality rate was brought about by the cooperation and mutual assistance of the four obstetricians who have attended or consulted on each of the breech deliveries at Lincoln General Hospital.

Dr. Calkins pointed out the fact that it was more important to have trained assistants present at the time of management of breech presentation than it was to have them present at cesarean sections. The minute a woman with breech presentation is in the delivery room, there are two obstetricians present to attend that birth. This rule applies to the general practitioner as well as to the specialist.

Cecarean section is a conservative procedure when dealing with contracted pelvis, relative disproportion, uterine inertia, and failure of the breech to descend. Elderly primiparas are candidates for cesarean section.

Gross fetal salvage will be increased as we learn more of the causes of premature labor and apply this knowledge to the problem of breech presentation.

DR. WILLIAM G. CUMMINGS, Winnetka, Ill.—The mortality rates reported have usually been higher than in most cephalic presentations. These figures vary considerably in different institutions, depending upon the management, including prenatal care and evaluation, and, also, probably, the criteria used for correcting mortality rates.

At Evanston Hospital, in a little over twelve years, ending in August of 1954, there were 18,130 births. Six hundred five, or 3.33 per cent of these, were breech births. Including babies that weighed over 2,500 grams, there were 3 fetal deaths, for a corrected rate of 0.49 per cent, as compared with about 1 per cent for all births.

In a smaller series of about six years, checked years ago, in babies 1,500 grams or over, the corrected rate was about 1.5, probably showing, more than anything else, the increased rate due to prematurity.

Also, in comparing the series of the same hospital in 1938, there is quite an improvement shown. At that time the corrected fetal mortality rate was 7.3 per cent, as compared to 3.5 over all births. I am not sure I know all the reasons for this improvement. Certainly, part of it is due, no doubt, to improved techniques, both in prenatal management and evaluation, as well as the technique of delivery.

In this recent series, of course, practically all of these babies were delivered by well-trained obstetricians. Forceps on the aftercoming head have been used much more frequently in the recent series than in the older series, and I am sure that is a great factor. Forceps were used in somewhat less than 10 per cent of the births in the series before 1938; they are now used in nearly 75 per cent of the cases. Cesarean section is used less frequently now than in the former series; in fact, our cesarean sections are only slightly more in breech presentation than for all births.

I am sure that anesthetics play an important part in the improvement shown. Certainly, it has been brought out in the other papers that breech extractions should have deep anesthesia.

None of us have made any particular effort toward external version. I think most of us had the opportunity of doing it occasionally, if it could be done easily. We have never had a policy of routine breech extraction, although we do not hesitate to do a breech extraction if there is some undue delay in the labor.

In breech extraction, I think that one of the most important points is to be sure of full dilatation of the cervix,

I think some other points which have been brought out before should be stressed. Certainly, in the technique of delivery, slight pressure on the fundus—if any—is important. Cerebral hemorrhages have been caused by undue pressure on the baby's head. Use of forceps on the aftercoming head is certainly recommended for delivery of the head.

DR. P. B. RUSSELL, JR., Memphis, Tenn.—I would like to mention the importance of one thing, in particular, and that is the question of acidosis. At the University of Tennessee we originated the work on acidosis in labor. Sometimes the question of acidosis is overlooked—too generally, I believe.

We feel that these patients—be the presentation breech, cephalic, or what—should be watched closely. They should be given fluids regularly. The bladder should be emptied regularly, either spontaneously or by catheterization, every four hours. Also, the urine should be examined, and the breath watched closely for any acetone odor, as well as the carbon dioxide combining power of the blood.

I doubt if there is one among us who has not had some difficulty, wondering what was taking place, finding a contraction or a retraction ring present, with the resultant death in utero of the fetus.

There is one other thing on which I would like to state my beliefs, and that is the question of external version. I feel it has a place. The question of placenta previa, however, should be kept in mind.

DR. EMERSON K. BLEWETT, Austin, Texas.—With better obstetric practices, the more uncommon causes of fetal death and injuries assume a more prominent position.

One of the rare but important attitudes of the breech presentation is hyperextension of the fetal head, with backward bowing of the spine which was described by Falls in 1915, and which he called "opisthotonus fetus."

On reviewing the few case reports in the literature, one realizes that this particular attitude appreciably alters the prognosis for the baby. Transection of the spinal cord, dislocation of cervical vertebrae, and dislocation of the tibia or the femur are accidents listed as occurring to the baby.

In 1950 I performed a cesarean section on a multipara at term, with ruptured membranes and an oblique breech presentation, with x-ray confirmation of a hyperextended head and spine after the membrane had ruptured. This infant developed normally.

In 1952 one of my associates delivered a multipara vaginally, without any difficulty, of an infant in frank breech presentation with a hyperextended head confirmed by x-ray before onset of labor. This infant sustained a cervical transection of the cord, and unfortunately, the infant is still living.

From our two-case experience and from the reports in the literature, we feel that routine x-rays should be taken of all breech presentations, and undoubtedly the hyper-

extension of the fetal head will be found more commonly. If the hyperextended head is found and it does not spontaneously correct itself, and external manipulation cannot flex the head, then elective cesarean section is recommended.

In conclusion, I wish to ask Dr. Smith if his one case of transected spinal cord was x-rayed prior to delivery, or if—following the death of the baby—x-rays were taken of the cervical vertebrae to determine the cause of the transected cord.

DR. CARROLL J. FAIRO, Cincinnati, Ohio.—I do not think the infant mortality figures really go far enough. I wonder how many of those breech babies showed an effect of spastic paralysis as a result of cerebral injury? I have never seen figures on the follow-up of breech babies, as to how many of them developed cerebral injuries.

My incidence of cesarean section is a little higher in breech cases.

I wish to ask the authors what their opinion is about a higher incidence of cesarean section in view of the fact that so many of these babies are later found to be spastic.

DR. L. A. CALKINS (Closing).—I purposely did not mention the use of external version in my paper. After all these years I have no conflict with anyone who wants to try it. I have no confidence in it, and very few of our patients have had version attempted. There were some others done, of course, but they do not appear in the paper because that remains cephalic presentation.

As to the follow-up on the number of spastic babies in this series, I have no knowledge. We do follow our babies for a time, and to my knowledge there has not been a case of cerebral spasticity.

DR. CHARLES J. SMITH (Closing).—The case of a fractured cervical spine was an instance of something that occurred 34 times in our series, and accounted for most of the cases of traumatic morbidity that these babies suffered. For example, 6 clavicles and 2 humeri, as well as the cervical spine, were broken in these babies. The autopsy on this infant did not disclose any developmental abnormality of the vertebral arch of the cervical spine, which is as far as I can go in answering the question as to what might have caused this baby's death. I cannot state with any certainty whether or not this baby had hyperextension determined by x-ray prior to the onset of labor.

Not all of our patients diagnosed as having breech presentations are x-rayed, particularly multiparas. Although this is a teaching institution, we do not apply these adjuncts of testing to all our patients.

As to the question of cerebral palsy, I am sure that Dr. Eastman will take that up a little bit later this morning. I cannot answer the discussant's question directly without referring to the pediatrics part of it for information on the follow-up of these infants, but, from a vicarious standpoint, from our experience in conjunction with the Chicago Committee on Cerebral Palsy, I can state that the incidence of cerebral palsy in the youngsters we see through this organization does not appear disproportionately higher in babies with histories of breech deliveries than it does with other types of presentations.

# RUPTURE OF THE MARGINAL SINUS OF THE PLACENTA\*

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BELIEVE rupture of the marginal sinus is a lesion that merits further illumination because it is a frequent cause of maternal hemorrhage and, in a sense, is a new complication of pregnancy. I will try to develop the two ideas that rupture of the marginal sinus is far from rare and that it has some of the quality of newness.

I know that many have doubts that there actually exists such a thing as a marginal sinus, let alone a rupture of the marginal sinus. It would be naive to think that any skeptic is going to be convinced this morning but possibly disbelievers and the hitherto disinterested will be persuaded to look for rupture of the marginal sinus. My experience has been that if men will look for rupture of the marginal sinus they will find it. The sinus itself has been described so many times in the literature of anatomy I do not feel that I have to defend its existence.

The reasons we can look upon rupture of this marginal sinus as a new lesion are several. I have learned that in some hospitals it is so new the diagnosis has never been made or, apparently, not even considered. From other hospitals I have news that rupture of the marginal sinus has only recently been sought for the first time and found. From the literature I sense that rupture of the marginal sinus is neglected in many places.

To the best of my knowledge, and of our record librarian's, the diagnosis of rupture of the marginal sinus never appeared on the face sheet of a patient's chart at the Charity Hospital in New Orleans until the second half of 1951. Prior to July, 1951, I had never diagnosed a case of rupture of the marginal sinus nor had I ever searched for one. My attention was called in 1951 to this example of morbid parturition by the publication of Fish and his associates.¹ It seemed to me this might be an important lesion that deserved more attention and better understanding. Therefore this study was undertaken.

Where had rupture of the marginal sinus been meanwhile? Or, better put, where had most of us been in relation to rupture of the marginal sinus? Possibly you have asked yourself, or will ask yourself, this question. If I ever heard of rupture of the marginal sinus before 1951 it must have been in a most unreceptive moment.

The diagnosis of rupture of the marginal sinus has not been acknowledged by a listing in the Standard Nomenclature of Diseases. It can be described

<sup>\*</sup>Presented at the Twenty-second Annual Meeting of the Central Association of Obstetricians and Gynecologists, St. Louis, Mo., Oct. 7 to 9, 1954.

and coded as, "Placental vessels, hemorrhage, cause undetermined" (79 × -Y00.7), or it could be, "rupture or perforation" (Y00.3), or "rupture" (Y00.5).

# History

I have not been able yet to piece together a continuous history of this concept of bleeding from a ruptured marginal sinus. Actually, it is far from being a newly recognized complication of pregnancy. It seems merely to have been overlooked for a few recent decades. The earliest article on rupture of this sinus that I have read is well over a century old. Jacquemier in France wrote about it at least as early as 1839.<sup>2</sup> He thought that rupture of a marginal sinus was frequent in normal pregnancy, in premature separation of the placenta, and in placenta previa. Something Jacquemier said is of interest to us today because it describes the experience I am reporting: "While I was at the Maternité, I examined with great care the placentas of almost all of the women who had had a hemorrhage, either during pregnancy or in labor. I have found in some clear proof that the loss of blood came from the circumference of the placenta without this showing signs of earlier detachment."

In Edinburgh both Duncan<sup>3</sup> and Simpson<sup>4</sup> wrote about it in the 1870's. They understood bleeding from the sinus at the placental margin to be one of the major causes of antepartum hemorrhage. From Paris in 1893 Budin<sup>5</sup> provided drawings that depict exactly what I am talking about this morning. The prominence and the number of the corroborators that these men mention suggest that bleeding from the marginal sinus was a widely used diagnosis.

What has happened to rupture of the marginal sinus in the intervening years I can only guess. Possibly the men whose textbooks and schools dominated American obstetrics in the first half of this century slighted it because they were more intrigued by abruptio and placenta previa. Some of our textbooks and the current literature convey the idea that the two most common causes of bleeding in the last trimester or semester of pregnancy are placenta previa and abruptio. We can have reason to suspect that this is entirely wrong. They may be the most important because they are the most dangerous, but I do not think they are the most frequent. A solid argument can be built for the claim that there are more common varieties of bleeding in this part of pregnancy and one of them is rupture of the marginal sinus. There is also a substantial group in which the cause of bleeding is never accurately identified.

# Anatomy of the Marginal Sinus

The marginal sinus of the placenta is a system of veinlike channels of great delicacy and thinness. These sinuses lie in the decidual tissue at the edge of the placenta and they discontinuously encircle the placenta. The name "circular sinus" has also been used. The lengths and diameters of the sinuses vary. The caliber is in the order of 2 to 5 mm. I have seen a sinus filled or, better perhaps, ruptured, and replaced by a finger of clotted blood that measured 2 cm. in diameter.

With experience you can identify the marginal sinus rapidly by incising into the placenta's margin. Perforations into the sinuses can be disclosed by peeling back the membranes at their placental attachment and wiping clean the edge of the placenta. I know that many have looked for the marginal sinus and have been disappointed. Some were mistakenly seeking an unbroken, uniform vessel that made a circle around the placenta. Actually the sinuses have no obvious intercommunications as viewed under the conditions imposed upon us, i.e., inspection of the maternal surface of the placenta, out of the

uterus and in our hands. Another reason for failure to recognize the marginal sinus is that when the fresh specimen is held in the hands with the maternal surface uppermost, the blood, still liquid, escapes from the sinuses, if it has not already done so; the walls of the sinuses collapse and their flaccidity makes it difficult to identify them. Parts of the marginal sinus may be left behind in the decidua at the time of the placental separation.

For class demonstration of the marginal sinus take two or three normal placentas and let them lie overnight in a refrigerator, not a freezer. Blood in the marginal sinuses at first is liquid and will remain in that state for some time. The next day, in the portions where the blood has not drained away, the sinus cavities can be identified by the casts of coagulated blood they contain.

These sinuses contain venous maternal blood and are part of the placentaluterine plexus that forms the maternal blood-collecting system. From these sinuses the blood passes to other decidual vessels, to the uterine veins, and hence into the mother's general circulation. Recent experimental work has confirmed that the blood in the marginal sinus is maternal blood.<sup>6</sup> In 1873 Turner,<sup>7</sup> in an exposition on the circulation of maternal blood in the placenta, could cite a formidable list of corroborators. He named the circular sinus as part of that circulatory system.

# Observations at the Charity Hospital

My own attempt to learn something about rupture of the marginal sinus covers three periods and two slightly different approaches. The first portion of these observations began July 1, 1951, with the collection and examination of as large a number of placentas as possible from the women with antepartum hemorrhage on the obstetric unit of the Tulane Service of the Charity Hospital at New Orleans. The study continued for one year and by a wide margin lacked being a continuous series of cases. In that fiscal year there were 4,103 deliveries on the Tulane Service. I identified 16 cases of hemorrhage as being due to rupture of the marginal sinus. These cases will be combined with others in my description of the syndrome.

In the first and third quarters of this year (1954) we were successful in gathering and categorizing by cause of bleeding the placentas from every case with antepartum bleeding on the Tulane Obstetric Service at the same hospital. Because there were 2,251 deliveries in those 6 months we can get some notion as to the frequency of the various causes of bleeding. The use of this number of patients might introduce some sampling errors so I do not claim that my incidences are any more than notions. I think they do hint that rupture of the marginal sinus is something big enough for us to give more thought to it.

During the intervals between the studies the diagnosis of rupture of the marginal sinus was made a number of times by the residents. These cases are not available for inclusion in this report.

I made my criteria for the diagnosis rather severe to encourage objectivity and to avoid errors inherent in any effort to find a place for a new or neglected subject. The sine qua non for diagnosis was the immediate postpartum exhibition at the margin of the placenta of a clot that was continuous with clotted blood in the marginal sinus. This is a stringent requirement and certainly some cases were discarded into the group in which no diagnosis could be made because the clot at the placental margin was dislodged in passage through the cervix, vagina, and the obstetrician's hands. The clot at the margin is usually not large and does not give the impression that it has interposed itself between

the placenta and the uterus. I would guess that the clot at the margin averages between 50 and 100 c.c. The clotted blood in the sinus is not difficult to find because this cylinder of blood is usually thick, appearing to burst from its confines. Conceivably there are cases in which the blood did not clot and which therefore are not included.

Table I shows the causes of bleeding in the 97 cases of uterine antepartum bleeding on the Tulane Obstetric Service of Charity Hospital in the first and third quarters of 1954. There were 2,251 women delivered on the unit in those six months. In that period there were 33 cases of rupture of the marginal situs, a ratio of one to 68 cases. There were only 6 cases of placenta previa and 13 cases of abruptio. The cause of bleeding could not be positively determined in 30 cases. Cervicitis, low-lying placenta, and a circumvallate placenta were less frequent causes of bleeding.

TABLE I. CAUSES OF HEMORRHAGE, 97 CASES IN 2,251 DELIVERIES

Rupture of the marginal sinus	33 cases	
Cause undetermined	30 cases	
Abruptio	13 cases	
Cervicitis	10 cases	
Placenta previa	6 cases	
Low-lying placenta	4 cases	
Circumvallate placenta	1 case	

I should define the qualifications that were needed for a case to be considered one of antepartum hemorrhage. Rather than base it on an estimation of the amount of blood seen, on which two persons rarely agree, I have included all cases in which there was enough blood loss that the patient's blood was typed and cross-matched, the facilities for cesarean section alerted, and then a vaginal examination performed. The qualification of preparedness for operation eliminates several cases of abortion, one of them a missed abortion. A case of bleeding from condylomas in the vagina is also excluded.

In each case of rupture of the marginal sinus the diagnosis of placenta previa had been ruled out by failure to palpate a placenta on vaginal examination. Abruptio was dismissed as a diagnosis when neither the placenta nor the clinical picture was considered diagnostic by the staff.

These inflexible criteria serve to prevent rupture of the marginal sinus at this time from being a diagnosis of exclusion or elimination. Such a diagnosis would be a bad start for our comprehension of a lesion that may be entering a renaissance.

#### Rupture of the Marginal Sinus

When you pick up the placentas and handle them to become better acquainted with the marginal sinus you will see that its delicacy and peripheral position make it vulnerable. It is easy to imagine that with the changes that went on directly under it there could have been a disturbance, a tearing, that permitted blood to escape. The changes in the uterus that could effect this were the uterine contractions, formation of the lower uterine segment, effacement, and dilatation. With slight traction on the membranes you can tear open some sinuses. This can be visualized in the photograph, Fig. 1. There is a possibility that inside the uterus the fetal surfaces make a traction in the direction of the cervical os. To these changes and stresses it appears that the edge of the placenta that is closest to the cervical os would be the most exposed and some data that support this conjecture will be presented.

Because that which transpired does so under cover, we will for the time being have to assume that blood escapes from the marginal sinus, dissects between the membranes and the uterus, and makes its way to the cervix. I think that we have collected enough indirect evidence that just that happens. It is not taking any more liberties with our imagination than we do with abruptio. We have seen the end results of abruptio but exactly how it transpired is a surmise. In some specimens I have seen a track the blood made on the chorion as it made its way from the sinus rupture to the opening in the membranes (and the cervical os).

The 49 cases of rupture of the marginal sinus that I have collected hardly give me the temerity at this date to state what the clinical picture of the syndrome is. Not many cases have been analyzed in the literature. There has been only one larger series of cases than mine and that contained but one more case. As I relate a description of my patients and what happened to them I unfortunately see no clues to a predelivery diagnosis of rupture of the marginal sinus. There were no trends discernible in the age or race of the patients. When more cases are collected this may turn out to be a complication of multiparity. Only 8 of the patients were pregnant for the first time and 37 per cent had been pregnant five or more times. The median length of gestation for these cases was 36 weeks. All except 5 women were delivered within two days of the onset of bleeding, so recurrent hemorrhage may not be a prominent feature.



Fig. 1.—Uterus with placenta in situ, showing marginal sinus. Eighth month of pregnancy. (Courtesy Dr. Harold Cummins, Department of Anatomy, Tulane University.)

Only 7, or 14 per cent, of these women with rupture of the marginal sinus had toxemia. On the same service it has recently been tabulated that in a period of one year 19 per cent of the patients had hypertensive-albuminuric disorders of pregnancy.<sup>8</sup> Thus at present it does not appear that rupture of the marginal sinus will be an added burden for toxemic women.

In all cases the bleeding was painless. Increase in uterine tone and tenderness to abdominal palpation were never demonstrated but it does not seem to be beyond the realm of possibility that a collection of clotted blood at a placental margin and between the membranes and the uterus will at some time cause pain. If someone starts putting leading questions to these patients we will presently have recorded that some of these patients have pain or tenderness. This type of history taking has often led to a diagnosis of abruptio where no abruptio existed.

In relation to labor, the bleeding appears to be anything but a late occurrence. In 31 of these 49 cases the bleeding began either shortly before labor, at the onset of labor, or early in the first stage of labor. Bleeding began in the second stage of labor in only 5 cases.

The form in which the blood appeared was in all the forms that blood can take. Bright red bleeding predominated. Clots and dark red blood were also recorded. Blood in different physical forms was often seen in the same patient.

No patient showed general signs of acute blood loss. In 5 instances it was believed the patient had lost over 500 c.c. In only 9 of the 49 women was the estimated blood loss less than 100 c.c.

The effect of rupture of the membranes is of interest in every type of last-trimester bleeding. I cannot say whether artificial rupture of the membranes will dependably control this bleeding because it has not been tried often enough. In 8 cases the membranes were already ruptured when the bleeding began. The height of the placenta in the uterus would seem to make tamponade

less likely than in marginal placenta previa.

Rupture of the marginal sinus gives promise of being less hazardous for the fetus than abruptio and placenta previa. This should not be surprising because the blood that is lost is maternal blood, characteristically is not great in quantity, and would not profoundly disturb the placentouterine union. One of my babies was a 26-week stillborn but the others did not give a distinct impression that as a group they were handicapped by the rupture of the marginal sinus. I have data only on the immediate postnatal state of the babies.

Thirty-six per cent of the babies in my series were premature by weight (2,500 grams or less). As the premature rate at the Charity Hospital is about 14 per cent there may be a significant relationship between rupture of the

marginal sinus and premature birth.

I have no indication that any other pathologic condition occurs with any frequency in association with rupture of the marginal sinus. There have been no cases of hypofibrinogenemia. The third stage of labor appeared unaffected. At another state charity hospital two of our residents operated on a woman because of a diagnosis of abruptio. Later they decided that the true diagnosis was rupture of the marginal sinus. Fifty per cent of the surface of the

uterus had the discoloration typical of Couvelaire uterus.

From the data I have, let me construct a picture of the hypothetical, typical patient who has rupture of the marginal sinus. She is a multipara and not yet at term. She may be of any race or age. Painless bleeding began close to the time she thought she went into labor. The amount of bleeding was not life-threatening. When I did a vaginal examination I learned that she was in the first stage of labor, the membranes were intact, and the placenta could not be palpated. It did not seem to be a case of abruptio but to play it safely I ruptured the membranes to hasten labor. Labor proceeded at a normal pace and there was enough bleeding to be a little worrisome. The infant to my relief did not appear to be affected by the hemorrhage. I delivered the placenta carefully in order not to dislodge the clots. I examined the placenta immediately and on the placental margin, at the side nearest the rent in the membranes, I found an elongated clot. This clot was attached to clotted blood in the marginal sinus.

## Bleeding of Undetermined Origin

In the table listing the causes of bleeding in a six-month period you may have been surprised to see there were 30 cases in which the cause of bleeding was unknown. In the 1951-1952 series there were 30 such cases documented

and, I am sure, many more undocumented. A digression may be in order for a moment on this subject, which is really not remote from our attempt to establish a place for rupture of the marginal sinus. I believe that bleeding of undetermined origin is a comparatively frequent occurrence and that it does not happen only at the Charity Hospital. It is an event that goes unnoted, unremembered, unrecorded in the literature, and unmentioned in the next day's doctors' dressing room conversation because of a failure to provide a dramatic quality.

When I read reports on the incidence and management of bleeding in the last trimester I am surprised that in so many papers all of the cases are neatly packaged into the various diagnoses. They are either able to make a diagnosis in each bleeding case or are omitting cases in which the diagnosis was uncertain. In some, if they have rupture of the marginal sinus, these cases are being diagnosed as something else or are among the cases unmentioned. I suspect many cases of rupture of the marginal sinus are being labeled abruptio, low-lying placenta, or placenta previa.

This classification of bleeding of undetermined origin is slighted in many reports because this diagnosis does not get on the face sheet, the first sheet, of the patient's chart and is therefore uncoded. There is a code for this diagnosis. This bleeding did not finally threaten the mother's life and did not kill the baby so when the time came in the record library to write the diagnosis it was forgotten. In my personal experience as a laborer in record libraries I learned that when a woman had bled at the end of her pregnancy and no placenta had been found over the cervical os by vaginal examination or at cesarean section the case was often called an abruptio, possibly a "mild" abruptio. In some medical communities "low implantation" may be popular. Contributing to this spurious extinction of the diagnosis of bleeding of undetermined origin is the feeling that such a diagnosis is an admission of professional ineptitude.

#### Comment

Could it be possible that the placenta with the rupture of the marginal sinus is the placenta with one edge not sufficiently low on the uterine wall to qualify for marginal placenta or low implantation yet is low enough to have its marginal sinus torn by the actions of the uterus in labor or in the preparation for labor? Some observations I have made tend to substantiate this. The location of the laceration in the membranes often suggests that the placental margin was not far away from the cervix. Also, if you will carefully examine any placenta and its membranes, taking care not to extend the rent in the membranes, you will see that this rent is usually not in the apex of the sac but is eccentric. This year in 18 cases of rupture of the marginal sinus we noted the relationship between the sinus rupture site and the tear in the membranes. In 2 of the sacs the rent was exactly at the apex but in all of the remaining 16 specimens the sinus rupture and the rent in the sac were on the same side. This observation seems to strengthen the concept of bleeding from the marginal sinus.

During these months of investigation into the marginal sinus 2 normal deliveries have occurred in which the placenta, examined immediately after delivery, had a large clot at its margin and that clot was connected to clotted blood in the marginal sinus. But there had been no bleeding at any time! In

other words it was the exact picture of rupture of the marginal sinus without the external bleeding. At first this was rather disconcerting but have we not always had cases of concealed hemorrhage in abruptio? So why not in rupture of the marginal sinus? A number of reasons could be postulated why the blood did not pry between the membranes and the uterus to the cervical os: e.g., all of the blood promptly clotted, the blood lacked pressure, the membranes were too adhesive, the distance from the placental margin to the cervix was too great, or there was not enough time. To learn if this symptomless variety of rupture of the marginal sinus was frequent 47 placentas, taken completely at random, were examined closely for evidence of this lesion and none was found.

It is natural that we should think of bleeding from the marginal sinus in terms of abruptio, placenta previa, and low implantation of the placenta because they are the conditions from which it will have to be distinguished. Jacquemier in 1839 pointedly warned against thinking that separation of the placenta had taken place when it was only a rupture of the circular sinus. A certain amount of blending of one of these placental complications into the other may be inevitable.

Abruptio at times has been a diagnosis to which cases have been assigned without sufficient justification. Abuse of the diagnosis of either abruptio or rupture of the marginal sinus can be avoided by strict adherence to definitions. As we collect more and more information about rupture of the marginal sinus and it attains the secure place in our teaching and practices that it deserves, what are we going to think about studies of abruptio that originate in institutions where the diagnosis of rupture of the marginal sinus is not made? We are going to think that some of the abruptions were ruptures of the marginal sinus! When groups of cases of abruptio are reported and the cases classified by the gravity of the condition of the mother, a large number, sometimes over 50 per cent, may be listed as "mild." Might not some of these be ruptures of the marginal sinuses? The practical importance of this is that, when we subtract these "mild" cases, abruptio becomes a more serious condition and possibly the indication for radical management is augmented.

We have been thinking of abruptio in terms of reports in the journals and in our own experience; in both of these backgrounds the cases of abruptio were diluted with cases of rupture of the marginal sinus. Because of the grave potentialities of abruptio it is important for us to learn more about rupture of the marginal sinus, separate it from abruptio, and reappraise abruptio in the light of our new information.

Is it possible that some cases of abruptio begin with rupture of the marginal sinus? The easiest way out for the blood would seem to be toward the cervical os, drawn there by gravity, a point of lower resistance, and the myometrial activity. Is it possible that when rupture of the marginal sinus occurs in some selected women, for example toxemic women, the blood might dissect under the placenta instead of between the membranes and the uterus? Could a placenta that is altered, for example the placentas of toxemic women, be one in which it would be easier for the blood to go under the placenta than else-

where? Infarcted placentas may not be as firmly attached as others and thus may permit blood to get under them. Only 6 placentas of abruptio have been closely examined for details of the marginal sinus and rents in the membranes. For 3 of them it was simply recorded that there were clots in some portion of the marginal sinus. In 3 more recent cases the clots in the marginal sinus were on the same side as the rent in the membranes. These few observations serve as nothing more than a stimulus to search further for a possible connection between abruptio and rupture of the marginal sinus.

The abnormally implanted placenta has a sinus that could be very easily torn by the changing shape of the cervix. There is really nothing new about this idea. It was all told in the last century. Jacquemier recognized the possibility. Seventy-five years ago Duncan described bleeding from the marginal sinus in a marginal placenta previa without detachment of the placenta. As the marginal sinus is only a part of the uteroplacental sinus network that bleeds in placenta previa this should not be difficult for us to accept. I have seen placentas from cases of marginal placenta previa that were indistinguishable from the placentas of rupture of the marginal sinus.

# Summary

Rupture of the marginal sinus is found to be the most common cause of antepartum bleeding during a six-month period that included 2,251 deliveries. The next largest number of cases of hemorrhage was in a group in which the cause could not be determined. Abruptio and placenta previa were less frequent causes of hemorrhage. The anatomy of the marginal sinus and some characteristics of its rupture are described. Many cases of rupture of the marginal sinus have been misdiagnosed as abruptio; there is a need to differentiate these two conditions.

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#### Discussion

DR. W. C. KEETTEL, Iowa City, Iowa.—There have been many excellent papers written concerning placenta previa and premature separation of the placenta; unexplained antepartum bleeding, however, although very common, has received little attention until recently. This increased interest in placental pathology directed toward ascertaining the cause of such bleeding is gratifying.

In the past the existence of the marginal sinus had been questioned, though now the majority recognize the sinus as an anatomical entity. Most agree that this sinus occasionally ruptures during pregnancy, producing varying amounts of vaginal bleeding.

The confusing issue then is whether marginal sinus rupture is to be considered as a new and distinct clinical entity, or should it be included as an occasional causative factor in the bleeding of the placenta previa and premature separation of the placenta. The essayist, along with Fish, feels that one can clearly distinguish between rupture of the marginal sinus and premature separation of the placenta. The criteria being: (1) the presence of a clot at the margin of the placenta that is continuous with clotted blood in the sinus, and (2) painless bleeding at term. They mention that at times the bleeding of placenta previa and premature separation may be caused by marginal sinus rupture.

It is hard for me to see how bleeding at the margin of the placenta, particularly where there is an adherent clot that may depress some of the marginal placental tissue, is materially different except in location from premature separation of the placenta. Where the membranes are dissected away from the decidua by blood because this is the path of least resistance, is this not really premature separation of the membranes and a form of placental

separation?

Two years ago before this Society, Dr. Paalman discussed circumvallate placenta and pointed out how frequently antepartum bleeding was encountered. He and others have maintained that the bleeding with this type of placenta is due to the fragility of the decidual covering of the marginal sinus. I wonder what Dr. Ferguson's experience has been concerning this point?

In our clinic and in others the diagnosis of premature separation of the placenta includes both the toxic and nontoxic type of separation. The diagnosis of the mild type of separation must not be construed as a "waste basket" diagnosis as the author mentioned. Naturally, with this broader concept, minor degrees of separation are recognized, and on occasion even though the bleeding is painless and the uterus is nontender, if the placenta shows significant signs of separation, they are included. Is it less exact to state that the bleeding is from placental separation which at times is due to sinus rupture than to state that marginal sinus rupture is a distint clinical entity?

Sexton, Hertig, Reid, and Harris have written concerning this problem and have felt that the rupture of the marginal sinus should be included as one of the causes of nontoxic placental separation. To me this seems more logical and will lead to far less confusion. The treatment by necessity must be the same as that employed in the management of mild nontoxic separation, since the diagnosis cannot be made until after the delivery of the placenta.

This presentation has been well organized and presented and I have enjoyed reading it. The paper emphasizes the following points: (1) There are many causes of antepartum bleeding. (2) The treatment of antepartum bleeding must be individualized according to the cause. (3) Abdominal delivery should never be resorted to for the treatment of undiagnosed antepartum bleeding. (4) Significant bleeding from the marginal sinus does occur.

#### THE PLACE OF OPERATIVE OBSTETRICS\*

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THE maternal, stillbirth, and neonatal mortality rates have not reached the irreducible minimum but the rates are so low it is obvious that other measures must be instituted if further reductions are to be made. These comprise: (1) improving resident training, (2) constant practice by the obstetrician, and (3) the appointment of one or two doctors on each obstetrical service to act as consultants for complications such as toxemia, abruptio placentae, placenta previa, prolonged labor, breech position, etc.

Our Board has established certain requirements for its approval of a residency but makes no inspection. It accepts the recommendation made by the Council on Medical Education and Hospitals of the American Medical Association, which the Director (Leveroos) states are based on the inspection report of the field representative, a detailed 4 page form furnished by the hospital (admissions, types and number of operations performed by staff and by residents) and considerable other data. The A.M.A. committee also has available the qualifications of the department head and others responsible for the residents' training. "This Committee may or may not accept the recommendation of our field representatives, in fact, frequently does not. It exercises its best collective judgment and makes recommendations for approval or withholding of approval to the Council. The official action then is a joint one, involving the two organizations."

The following excerpts are from Essentials of Approved Residencies and Fellowships of the American Medical Association revised to June, 1954: "A hospital must have been previously registered by the American Medical Association and approved by the Joint Commission on Accreditation of Hospitals." The organized staff must consist of ethical licensed physicians holding the degree of doctor of medicine from approved medical schools. There must be an educational committee of the staff which is responsible for the organization, supervision, and direction of the residency program.

The residents should receive ample instructions in antepartum care, treatment of toxemias of pregnancy, management of normal and abnormal labor, technique of versions, breech extractions and instrumental delivery, diagnosis and treatment of the complications of labor, postpartum hemorrhage, puerperal infections, cesarean section, etc. An admission rate of at least 400 patients a year is desirable in each of the fields of obstetrics and gynecology.

I was assured by the Director that the committee take into account the number of deliveries, incidence of operations and complications in arriving

<sup>\*</sup>Presented at the Twenty-second Annual Meeting of the Central Association of Obstetricians and Gynecologists, St. Louis, Mo., Oct. 7 to 9, 1954.

at a decision only as to whether or not the service can provide a sufficiently broad experience to warrant approval for resident training. The determination as to the number of residents is made at the hospital level—not by the Council or the Board.

Over the years a number of our instructors and professors and many doctors on our courtesy staff have had their training at other institutions. We have noted that those men who had been trained on services which had a low incidence of operations and complications lacked skill to such an extent that babies and mothers were injured or died as a result of their lack of training or of their incompetence.

One departmental head stated that he was amazed at the large number of institutions that are approved for residency training and also after two sessions as associate examiner of the American Board, he was upset by the inadequacy of some of the candidates. He stated, "I am convinced that obstetrics and gynecology are surgical specialties." Leveroos commented that "the mere fact that there are a large number of hospitals approved for resident training is not, I believe, of any particular significance. Over 90 per cent of residencies in obstetrics-gynecology are currently filled. Should the number of approved hospitals be appreciably reduced the number of residents who could receive training would be, of course, curtailed. One might question whether such an approach is altogether sound. If the objective of residency training is to produce a limited number of highly trained specialists, the department head would have a point. I believe, however, that the public interest is better served in having a relatively large number of younger men receiving advanced training, even though some do not receive the type of educational experience which your department head would consider optimal. I would like to point out that medical schools as well differ in the level of education provided, which is not to argue, in my opinion, that we should, therefore, reduce the number of approved schools."

So far as I can determine, there is an idealistic pattern for training residents in our specialty, but there is nothing specific. No detailed attention has been given to the method of teaching, that is, on the manikin, on the patient, or on both, the percentage of operative procedures, abnormal cases, complications, etc. Thousands of deliveries are of little value in training if nothing is done with them and if there is no careful supervision. I realize that some men learn easily and are adept with their fingers. Some men teach quickly, some teach slowly, and some cannot teach. Douglas in 1954 pointed out some of the faults of resident training. He stated, "The Chief of a service should feel the same sense of responsibility to his house staff that he does to his own family. Actually they are temporarily his children and they should look upon him as a father, a guide, counselor and an example they can follow."

The data published by the American Medical Association and by hospitals for prospective residents list the number of obstetrical beds, bassinets, deliveries, and the number of clinic visits, but few publish the number of opera-

tive deliveries and complicated cases. It is obvious that if all patients are delivered spontaneously there is very little opportunity for the residents to learn the technique of operative procedures.

I had my training in a hospital where the incidence of operative deliveries was 67 per cent. The incidence of operative deliveries at the Chicago Lying-in Hospital in 1931 was 33 per cent. This figure has increased until it is now 80 per cent. I realize that many of you in your private practice have an operative incidence of almost 100 per cent and your results are excellent. I will show that our results are far better under a high operative incidence in which the men are trained to perform these various procedures under supervision than it was under the lower operative incidence when various subterfuges had to be used for indications and the men were not so well supervised. Some residents even refused supervision, stating that they could learn only by trial and error

I have been engaged in full-time clinical obstetrics and gynecology since 1922 and have helped train many men in our specialty. In retrospect, I am far from satisfied as to the degree of skill they attained during their residency.

My state license grants me the right to practice medicine which means that I may perform any operative procedure that the hospital will permit. I have never been examined as to my ability to perform these procedures and I will never in the future be examined as to how proficient I still am. Assuming that I once had the skill properly to perform these operations, does this skill persist if not practiced? The answer is "No," but how many doctors try to rectify this? The doctor practices golf, tennis, chess, card playing, skeet shooting, etc., but he does not in most instances practice the procedures used in his specialty. The work of the sanitary engineer (plumber), electrician, etc., is subject to periodic surveys by some appointive authority and the plumber or electrician who has not worked for ten years and then returns would find many changes which he would be compelled to accept. The medical profession has always been one of the most highly regarded professions. The doctors have always had unusal powers and have not abused them. The specialist, however, must maintain his skill and he must constantly improve his results. If he fails to do this, the hospital administration, the local board of health, or some other authority will intervene.

If we grant that a high operative incidence and many complicated cases are required for training residents, (a) are we justified in performing elective procedures such as low forceps delivery, version and extraction, manual removal of the placenta, packing the uterus, etc., for training; (b) how can we protect the patient and baby in elective procedures?

How many cases of operative delivery, manual removal of the placenta, and other procedures does a man have to assist at and/or perform to become expert in their use and how many must be perform each year while in practice to maintain that proficiency.

I sent questionnaires to our staff, our residents, and the heads of 34 obstetrical services, asking if they would list the minimum number of the vari-

ous operations and complicated cases for ideal training in a three-year period and the minimum number which the specialist should practice each year. I appreciate the courtesy of the 28 doctors who answered the questionnaires or sent explanatory letters (6). I have summarized these data in Table I, A. No statistical analysis of the material was made but I believe that some organization must make such a study if resident training is to be improved. There is marked variation in the range both for training and practice in the figures given by the professors and the resident group.

TABLE I, DATA ON VARIOUS OPERATIONS AND COMPLICATIONS FOR TRAINING AND PRACTICE

		A. Fig	ures Fron	n Questio	nnaires		hor's Te Figures	entative
		PROF	ESSOR	RESI	DENT	TRAI	1	
		RANGE	AVERAGE	RANGE	AVERAGE	ASSIST	PER- FORM	PRAC-
Forceps delivery	Train	20-720	195	100-500	239	240	180	24
- stocks don't st	Practice	0-100	52	15-250	73			
Breech extraction	T.	5-35	151	10-250	105	50	12	6
	P.	1-8	6	5-30	12			
Version and extrac-	T.	1-15	6	4-40	15	50	12	6
tion	P.	1-4	2	1-25	6			
Cesarean section	T.	3-25	33	5-40	27	50	12	6
	P.	1-12	4	2-25	8			
Cesarean hysterec-	T.	1-8	4	2-50	13	12	3	1
tomy	P.	1-4	2	1-25	6			
Manual removal of	T.	1-50	31	12-100	45	50	12	12
placenta	P.	1-12	4	2-100	33			
Prolonged labor	T.	12-200	38	1-75	26	100		12
Totoliged labor	P.	1-40	10	2-20	6	100		
Eclampsia	T.	1-30	9	2-125	28	12		6
ciampsia	P.	0-1	9	2-12	5	12		U
Nonconvulsive	T.	10-80	37	18-300	87	100		12
toxemia	P.	3-10	7	1-50	20	100		12
Abruptio placentae	T.	3-25	11	10-200		50		6
	P.	3-23 1-5	2		44	90		0
Placenta previa				1-40	10	=0		0
	T.	5-50	15	10-75	27	50		6
	P.	1-5	2	1-12	5	700	20	0.4
Incomplete abortions	T.	5-100	40	25-150	61	100	20	24
	P.	5-20	10	2-35	16			
Shock and "cut-	T.	4-35	12	2-75	16	100	50	24
down'	P.	1-3	2	1-12	3			
Craniotomy	T.	1.5	2	1-10	5	12	2	2
	P.			1-3	2			
Dührssen's incision	T.	1-20	4	2-30	10	24	6	6
	P.	1-4	2	1-10	4			
Uterine pack	T.	2-20	9	2-50	17	50	12	6
•	P.	1-10	4	1-12	5			
Vaginal examina- tion:								
Late pregnancy	T.	5-300	10	10-410	147	400	400	50
1 6	P.	5-75	34	2-125	52		*00	
Labor	T.	50-500	204	12-500	183	400	400	50
24001	P.	20-90	47	2-100	34	400	300	00
Induction of labor	T.	10-50	25	10-175	50	100		50
induction of labor	P.	1-6	5	1-50	12	100		00
Anesthesia:	1.	1-0		1-90	12			
Local	T.	10-100	41	10-250	54	100	25	12
110041			11			100	25	12
G-:1	P.	2-20		5-75	21	100	0.5	10
Spinal	T.	15-300	68	20-300	87	100	25	12
* * * * *	P.	1-50	17	5-100	31		400	
Inhalation	T.	10-300	10	25-250	96	200	100	12
	P.	24-50	37	2-300	52			

Leveroos comments, "As a matter of principle the Council has attempted to avoid setting any arbitrary figures as to number of operations, deliveries, etc., as a requirement for approval. The quality of training, albeit much more difficult to evaulate, is, I believe, of considerable more importance that the quantity of material to which the resident is exposed. The minimal ranges, however, can serve a useful purpose as a rough guide in attempting to determine whether the experience in a department would be sufficient to justify considering it a suitable place for residency training."

One professor states: "Dührssen incisions, craniotomy and eclampsia in Northern States are so rare that no self respecting department could hope to give adequate training in their performance. The number of conditions which are too rare to make maintenance of skill for the practitioners possible is considerably larger." Another states that "practically all the younger men are given an opportunity to exercise their training at the city hospital."

Some of the professors thought that one could not use actual figures for these various procedures but they had nothing else to suggest which could be used for measuring the value of the resident training. Several professors stated that the treatment of shock and cut-down were interns' work. If they had had a patient die because a resident did not know how to expose a vein in a patient in deep shock, they would agree that this is work requiring the highest skill. Much of my research has required repeated venipunctures and frequently the patients have complained to me because of the lack of skill of one of the residents. Obviously one or two craniotomies, one or two Dührssen's incisions, one or two cut-downs or manual removals of the placenta are insufficient for training but they are better than none. Only our chief residents who are in their fourth or fifth year attain anywhere near the average figure which I have listed in Table I, B. During their three or four preparatory years, they have had the opportunity of maturing. They have seen their own mistakes, those of their colleagues, and those of the staff. During their final year they will make mistakes but I have always felt that it is better for a resident to rupture a uterus during his period of training than when he is in private practice. In the former period there is someone competent to help him save the woman's life and thereafter he is a better-trained and safer obstetrician. I do not imply that rupturing the uterus should be part of the resident training.

The minimum number of operative procedures and complicated cases which the resident should assist with or perform during a minimum period of three years' training are listed in Table I, B. "Assist" means as first assistant to an obstetrician or the resident supervising a junior resident. Teaching is a great stimulus for increasing knowledge and skill. Residents assist in the care of patients with obstetrical complications; they do not have complete charge of the patients. Finally, I have listed the minimum number of these procedures which the specialist should perform each year. These are tentative figures based on the possibilities on our service. I do not know the correct figures but this problem should be investigated further and some basic data acceptable to most of us will result.

The change in our operative incidence is shown in Fig. 1 and Table II. Our incidence of forceps delivery is 70 per cent. The midforceps rate has decreased markedly. Forceps delivery requires teaching and practice, a very definite knowledge of fetal and pelvic anatomy, of physics and of engineering. The man must also be adept with his fingers. Some men never become proficient with forceps. We have discarded the original idea that the forceps should only be used when the mother cannot deliver the baby and now use it to spare the mother the final pains of delivery and to spare the baby's head from the extra molding and pressure incidental to another one to two hours necessary for its passage over or through the pelvic floor. The majority of the mothers prefer this method. The baby cannot tell us whether he appreciates the shortening of the second stage but the results indicate that we are not doing any detectable damage. If any of you have been reading the various reports on cerebral physiology for both normal and abnormal conditions, you will appreciate the safeguards that nature has placed about the newborn baby so that its brain can stand the changing pressures and lack of oxygen. I wonder why any of them survive and, if they do, why the number of idiots is not greater than it is. There have been four recent reports in which the babies were studied two to thirty-one years after natural delivery, precipitate delivery, prolonged labor, and forceps and difficult forceps, precipitate labor meaning a duration of less than two hours. There was an increased loss of babies in patients with prolonged labor and forceps or with difficult forceps, but if the babies survived the neonatal period there was a lower incidence of serious eye defects and mental disease in the babies born by natural labor or after prolonged labor and forceps than by precipitate delivery.

TABLE II. VARIOUS OBSTETRICAL STATISTICS, 1931-1954

	1931-1940	1941-1945	1946-1950	1951-1954
Deliveries	27,321	17,520	19,902	11,208
Forceps	. '			,
Low	28.2	44.2	68.2	68.1
Mid or high	3.9	2.6	1.6	1.6
Version and extraction	1.5	0.7	0.6	0.5
Cesarean section	5.3	4.2	4.1	4.0
Cesarean mortality	0.69	0.12	0.1	0.17
Cesarean hysterectomy	0.4	0.6	1.1	1.1
Dührssen's incisions	1.9	1.1	1.0	0.1
Maternal mortality	0.252	0.068	0.04	0.064
Stillbirths-1,000 grams and over	1.9	1.3	0.9	1.0
Neonatal deaths—1,000 grams and over	1.7	1.3	1.1	1.10
Birth trauma, autopsy	0.53	0.12	0.09	0.05

A breech position in labor has always been associated with increased still-birth and neonatal mortality and some increase in maternal mortality. A "masterly inactivity," "hands off," "give nature time," or "watchful expectancy" does not improve results. If one knows what he is watching for, this type of treatment is excellent but I have seen mothers and babies die who had "watchful expectancy," etc. A somewhat comparable condition

occurs at our maternal mortality meetings when I question prenatal treatment which the investigator states was adequate but the patient is dead. viously the breech which advances fairly rapidly is not going to give much trouble in most instances. However, we recently had a primipara who delivered at home without anyone in attendance. The head stuck, resulting in a stillborn baby. One must know something about the progress in breech delivery and be able to interfere if it is not progressing normally. The reason for the high perinatal mortality is that there are too few breech deliveries during a residency or during private practice and the doctors do not maintain their skill by performing elective version and extraction. Goethals showed in 1939 that if all the breech deliveries in the hospital were performed under the supervision of one man, he not necessarily delivering the patient but supervising those cases in which he was not the operator, there would be a marked reduction in the perinatal mortality. This procedure should be practiced on all obstetrical services not only for breech but for toxemia, hemorrhages, abortions, etc.—that is, wherever the incidence of a condition is small. uncorrected stillbirth and neonatal mortality in 1946 for breech delivery of babies weighing 1,500 grams or more was 6.8 per cent and the corrected was 3 per cent. A recent unreported study gives 4.9 per cent for the uncorrected and 1.4 per cent for the corrected.

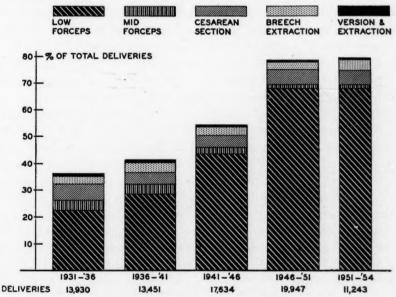


Fig. 1.—Shows the change in operative incidence.

Our incidence of intracranial injury as found at autopsy has diminished over the years, despite a constantly increasing operative rate.

Cesarean section has become a relatively safe procedure and yet carries a higher maternal mortality than vaginal delivery. This is caused by the increased hazards of pulmonary embolism. Early ambulation has not decreased this mortal danger. The incidence of cesarean section ranges from less than 1

per cent to as high as 10 per cent. We accept the fact that the rate has increased during the past decade primarily because of the increased safety which I attribute to better training and not to the use of antibiotics. Cesarean section is supposed to be a lifesaving measure for the mother and to ensure her a live, healthy baby. Strangely enough, with the increased incidence the still-birth and especially the neonatal mortality for cesarean section has not decreased but has actually increased. Our cesarean neonatal mortality in the last three years for babies weighing 1,000 grams or more is 4.4 per cent. During the past three years there were 451 cesarean sections with 25 neonatal deaths of babies weighing 1,000 grams or more. Hyaline membrane and resorption at electasis were found at autopsy in 16, 64 per cent, of the 25 infants that died in the neonatal period. This should be a preventable condition.

We became so concerned two years ago that we decided not to perform the elective cesarean section at 38 weeks but rather to permit the patient to go into labor. Our third death from aspiration pneumonia during a breech delivery made us reconsider the question of permitting a patient who is to have a laparotomy to come to operation without any preparation. My practice for the last eighteen months has been to perform the cesarean section as soon as the vaginal portion of the cervix has disappeared. The patient takes 8 Gm. of ammonium chloride per day for four days prior to operation and is restricted to 1,000 c.c. of fluid for the 24 hours preceding the operation. In addition, the patients have been given an oral diuretic. This dehydration procedure is an attempt to imitate the dehydration which occurs during normal delivery amounting to 1 kg. or more. The mean weight loss in 45 patients was 1,100 grams. There have been no neonatal deaths due to hyaline membrane in the infants of patients who were dehydrated. The series is small but it is a harmless procedure and may be lifesaving for the baby.

Our rate has been constant, but we have increased the number of cesarean hysterectomies either to remove an infected or potentially infected uterus or to remove a uterus after a woman has had her family, especially if she is in the late thirties or older. We have shown that cesarean subtotal or total hysterectomy is not a formidable or shocking procedure. Each resident who finishes on our service is competent to perform this operation within a minimum of time. There is still present an irreducible mortality associated with cesarean section—that due to pulmonary embolism. The death of a patient who has an elective cesarean section or the operation early in labor and who dies from puerperal peritonitis is, I believe, a preventable death which should be charged to the surgeon and operating-room procedures. Autoclaves must be tested periodically to determine whether or not they are effective. Several reports have been published reporting relatively small series of infected or potentially infected patients in whom cesarean section did not result in maternal deaths. The results were attributed to the use of antibiotics, parenteral fluids, and blood transfusions. This does not mean that patients should be permitted to be in labor for days or to have attempts at delivery and then be subjected to cesarean section. I do not subscribe to trial forceps or to gentle trial forceps. I do not know what either procedure is. I believe that the properly trained man can determine on vaginal examination, which is done if necessary under anesthesia, whether or not he can safely deliver the baby with forceps. If he is in doubt, he should have consultation with someone who can determine this fact.

The procedure of version and extraction is in disrepute because of the high maternal mortality from rupture of the uterus, but if these cases are investigated, in almost every instance it will be found that the operator was inexperienced. He did not know that there must be complete dilatation of the cervix, there must be surgical anesthesia, and the uterus must be relaxed. The procedure should be used or it should be discarded.

Dührssen's incisions are still a debatable procedure—debatable as to whether one prefers to incise a cervix, dilate it manually, or permit it to be lacerated spontaneously. We believe this procedure has its place when there is a rim of cervix left and the biparietal diameter of the head is through the inlet. We teach that Dührssen's incisions with dilatation of 5 or 6 cm. are indicative of an error in judgment.

Craniotomy is occasionally necessary even in the best institutions. It is inexcusable to perform a cesarean section because the baby is hydrocephalic or for the purpose of removing a hydrocephalic head which had separated from the body.

The placental stage is still a bugbear for many doctors, primarily because they were not properly trained in its management. The practice of waiting from thirty minutes to several hours for the separation and expulsion of the placenta is wrong. All studies show that the placenta separates as the baby is being delivered, and, if the man has been taught properly how to deliver the placenta or, in the exceptional case when this does not occur, how to separate it and deliver it, he loses his fear of this complication. All of our residents perform elective manual separation and removal of the placenta.

I am not entering into a debate as to whether or not the postpartum uterus ever requires packing. If one reads protocols of patients who die from postpartum hemorrhage, however, almost invariably the uterus has been packed two or more times by different individuals. It is of the utmost importance that the first packing be properly placed and be sufficient in amount but not excessive.

Induction af labor has its place in the treatment of toxemia, placenta previa, and abruptio placentae. Should it be used for the convenience of the doctor or the patient? Is it better for her to have a delivery under ideal conditions by you or a rapid delivery in a taxicab or in the hospital after a meal by intern or resident? Some of us learned obstetrics by means of repeated sterile vaginal examinations in late pregnancy and during labor. I do not know if any, women's lives were saved by the furor for rectal examination which began in the twenties and still persists on many obstetrical services. It has certainly resulted in some fetal deaths and possibly some maternal deaths. In general I believe it is unwise to induce labor in the normal patient unless you can recognize a "ripe" cervix. If one can recognize a "ripe"

cervix and the patient lives a considerable distance from the hospital, it is better for her to enter the hospital the night before for induction of labor and delivery the next day, with careful preparation in so far as omitting food and fluid for at least eight hours before delivery is concerned.

Table III lists the incidence for various operative procedures as well as other pertinent data for a recent period at our hospital, the New York Lying-In, Cook County Hospital, and the average for 52 Chicago hospitals. Our maternal, stillbirth, and neonatal mortality figures compare favorably with those of the other institutions. Our incidence of birth injury is no greater. Our incidence of operative delivery is much higher than that of any of the other institutions, but so far as we can determine we have done no harm to baby or mother. Our uncorrected figures for maternal, stillbirth, and neonatal mortality show a constant reduction.

TABLE III. COMPARISON OF OBSTETRICAL STATISTICS FROM SEVERAL HOSPITALS

4 *	CHICAGO LYING-IN 1951-1954	NEW YORK LYING-IN 1952-1953	COOK COUNTY HOSPITAL	52 CHICAGO HOSPITALS
Deliveries	11,208	8,110	10,503	78,919
Forceps				
Low	68.1	24.0	8.8	26.0
Mid and high	1.6	4.7	1.5	1.4
Version and extraction	0.48	0.17	0.33	0.24
Breech extraction	4.0	3.1	0.1	1.64
Cesarean section	5.3	4.8	2.42	3.67
Dührssen's incisions	0.1	0	0	0
Induction of labor	1.5	0	6.84	4.0
Manual removal of placenta	3.9	0.70	0.85	1.34
Uterine packing	0.4	1 pt.	0.05	0.34
Craniotomy	0.2	0	0.11	0.05
Mortality (%)				
Maternal	0.064	0.10	0.05	0.04
Stillbirth	1.00	1.10	1.90	1.57
Neonatal	1.10	1.00	2.87	1.91
Birth Injury	0.05	0.17	0.54	0.41
Premature delivery	6.6	6.9	14.4	8.3
Neonatal mortality (%)	10.4	10.0		

I have always thought that the patient should be treated as you would want one of your own family treated. One doctor thinks he is practicing conservative obstetrics by using no forceps but when the baby dies from intrauterine asphyxia or is born with a damaged brain, I wonder what he means by conservatism. Another doctor is accused of being radical because he does not permit his patients to be in labor for two or more days and terminates most deliveries by a low forceps. We have all seen conservatism that resulted in death and we have seen radical treatment which also resulted in death. Some doctors "do nothing," some "do too much," and few "do right." All of us make mistakes and I have made my share. Fortunately, Nature manages

expertly, provided obstacles are not placed in her way, such as too much or too early sedation, the wrong anesthetic, the wrong operation, a damaged forceps, etc.

Bank examiners make monthly inspections and I am told some of these inspections are made without warning. I think every obstetrical service should survey their results annually and preferably more frequently. Our record rooms have become a place for filling out insurance forms. The record room librarian should be the examiner for the medical staff. She should keep a minimum amount of pertinent data about mothers and babies which should be presented to the staff each month.

# Summary

Operative obstetrics when properly practiced is a lifesaving measure for mother and baby. When improperly performed it may result in death for one or both or lifelong injury.

To become trained, the resident must have the opportunity of assisting with or performing various obstetrical operations under direction. It does him no good to perform them without guidance. Certain minimum standards are suggested for training residents in a three-year program.

Certain minimum standards are suggested for the number of operative procedures which the trained obstetrician should perform each year to maintain his proficiency.

Comparative data from several obstetrical services are presented to show that a high operative incidence under proper supervision does not result in an increased maternal, stillbirth, or neonatal mortality or morbidity, but actually results in a decreased figure.

The hospital record librarian should be the examiner for the doctors and should each month furnish them with data as to the incidence of various complications and operations and of the maternal, stillbirth, and neonatal mortality.

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#### Discussion

DR. WILLARD M. ALLEN, St. Louis Mo.—I cannot recall if our own statistics appeared on that excellent summary. Dr. George Wulff was sitting next to me this morning, and it was he who analyzed our figures on breeches. He said to me, "You know, the ward statistics are as good as the private statistics." Naturally, that makes the chief of the service feel fairly good when his house staff can handle the breeches as well as the attending physicians. I do not know whether that means that perfection has been reached or not. I'm sure it has not.

I wish to comment about cesarean section. We have recently analyzed our own figures over a five-year period, and our incidence was approximately 3 per cent. It is a little higher among private patients, and a little lower among ward patients. As you see, this is appreciably less than the incidence at, say, the Chicago Lying-in Hospital.

The thing that has disturbed us about cesarean section has been the high fetal mortality. The fetal mortality among our cesarean section patients was nearly 9 per cent. In a similar study carried out nearly twenty years ago, the mortality of babies delivered by cesarean section was only about half of that. That sounds as though we should not do so many sections.

The real truth, however, is to be found in the indications for the cesarean section. In previous studies, many patients were delivered by cesarean because of purely medical indications, such as tuberculosis, heart disease, and a few other rare situations, whereas, in the present analysis, indications are that very few of our patients were delivered by section because of medical indications. The three indications are disproportion, placenta previa, and premature separation of the placenta. That is aside from the point of discussion as to how many patients a resident should deliver by any of the various operative means.

I do not believe that the larger teaching institutions can, by any means, train all the people who are going into obstetrics. On my own service I am able to turn out three to four people per year who are qualified for certain cases. Our hospital is one of the larger ones, and yet the residents actually complain on my service because they do not get enough operative obstetrics, especially cesarean sections. Even if we were tending to be a little more liberal, they still would not do fifty sections. It would be virtually impossible, because we do only, roughly, a hundred a year, and half of those are on private patients.

Therefore, I think we have to compromise, because my own feeling is that it is worth while to have obstetrics in the country done—in so far as possible—by men trained for it.

The only thing I would add is that I believe there is plenty of opportunity for men to be further trained after they complete their residencies. Every man in this room knows he has learned a great deal about the practice of obstetrics and gynecology since he finished his residence, and perhaps the best thing we can train our residents to believe is that even though they may have done a fair number of all of the operative maneuvers, they certainly cannot acquire all the judgment they need in the period of time they spend with us. I, for one, think they should learn to lean on older men in their communities, because there is not any field of medicine I know of where experience really counts for so much as it does in the specialty of obstetrics.

I do not feel bad that we cannot train our men to perfection. If we did, they would not be any good afterward, because they would not be able to learn anything after they had finished.

DR. HAROLD A. OTT, Royal Oak, Mich.—I speak a bit timorously, because I represent a small hospital. We do approximately one-fifth of what is done in the Chicago Lying-in. We have residents for training purposes, and we think we do a good job, or at least that is what the residents tell us after they get out, and that is what other people from the communities to which they go also tell us.

I think Dr. Dieckmann has raised a very important question here on how we can adequately train our residents. I think we recognize first that the problem is that there are not enough training institutions to train physicians adequately to take care of patients in obstetrics in the way in which they should be taken care of. Second, how are we going to train them, principally with private patients as material?

The problem in most cities—and in Detroit, from which I come—is the high percentage of private patients and the constantly dwindling number of clinic patients. Insurance and labor benefits have reduced the amount of available so-called teaching material. It has become rather axiomatic now in certain of our institutions that all patients admitted to the hospital are teaching material. I think it should be so.

One of the little complications that has arisen has been the attitude of one of the examining groups in talking about so-called "ghost" operative work. It was defined, I think, as any work done by someone not known to the patient as being the one who does the work. Actually, our residents do a considerable amount of work in these various procedures; they have to, in order to be trained. I must emphasize that this is always done under supervision.

I am glad to see that this criticism has been rescinded, so if the man who is the assistant does part of the work, under supervision, it is no longer classified as "ghost" work. But I think that is a concept that we have to keep in mind, and perhaps clarify a little bit more, so that we do not have bad public relations.

Of course, the problem of continuous training after residency work is very important; we team up a junior and a senior. This is a very good way of continuing the training on procedures that are rather rare.

We have learned a great deal from our monthly stillbirth and neonatal death conference. We learn more from our stillbirths, from an obstetrical point of view, than we do from our neonatal deaths. This has also had one other advantage that I am very pleased about—we are now getting the pediatrician into the delivery room in certain cases where we anticipate trouble. For example, in the case of the diabetic patient, the woman with the hypertensive disease, and abruptic placentae and so on, when we have a baby that we can salvage, and delivery is under way, it has been a hard job to get them out of bed at three o'clock in the morning. However, we have succeeded by merely saying, "Now, if you do not do this sort of thing, how can I depend on your going out and making a house call on a patient that I may refer to you?" It may be nasty business, but it is a way of getting results.

The other thing that has to be watched, too, in training (and this is a scheme that we like to do as much as we can) is the management of the so-called obstetrical emergency. We have developed a so-called emergency team which includes all the residents available at the time plus those we can call as quickly as possible, plus one or two other people, particularly our medical anesthesiologist. We have an anesthesiologist, and we're very glad that we have him.

We periodically review the so-called emergency type of cases, and we have learned a great deal about what to do within the first three or four minutes, because that is very frequently a critical period. We find that type of conference has been very, very useful.

I am not sure of the place of version and extraction in the training program. I think that many of these can be very lethal. I would like to go along with Dr. Dieckmann, and I think we should all have it in our armamentarium, but the use and the indication should be selected with extreme care and very emphatically stressed.

DR. WILLIAM P. SADLER, Minneapolis, Minn.—I was very much interested in Dr. Dieckmann's presentation of this teaching problem, and I want to bring up a situation as it exists in different communities.

My department at Minneapolis General Hospital—which is connected with the University—rather recently got a going-over by Dr. Norlander and the Committee on Hospital Accreditation. I think we came through it very nicely.

One of his objections concerned the volume of the work that we have. I have been connected with the institution for thirty years, and one of our problems, Dr. Dieckmann, is too much good times and prosperity. The volume of our work has gone down as the economic status of the people has gone up.

I think the time will have to come, if prosperity still continues, when we will have to work out an agreement between the private hospitals and our public institutions and at least rotate our men through a ward where they can see a larger volume of work than in the private hospital.

I was a student of Dr. Williams, Dr. Dieckmann, and was there a long time, and, as you know, he was quite conservative, but in recent years I have gone along with your idea of letting our young men do work electively, just in order to teach them. You cannot get around experience, but let's not give up the Dührssen's incisions—once in a coon's age it is very valuable.

DR. P. B. RUSSELL, JR., Memphis, Tenn.—In 1932 I was at Chicago Lying-in. At the time a study was instituted to see if there was any relationship or possibility of rela-

tionship between operative procedures in prolonged labor and the possibility of cerebral palsy or any injuries to the brain whereby the individual would be handicapped. I would like to ask Dr. Dieckmann if he has any statistics concerning this study.

DR. DIECKMANN (Closing).—As far as Dr. Allen is concerned, I do not think that any of us could turn out a perfectly trained resident, and even if we could, three or four or five years is still a relatively short time. I am still learning obstetrics, more than I am learning gynecology. I do not think you ever stop learning obstetrics. There is always something new.

I was pleased to learn from the discussant from Detroit that they are using teams, even an emergency team for treatment for shock. It is a step in the right direction; more of it will have to be done.

He raised the question of private patients, and that is a question that is becoming more and more important.

Douglas, in his discussion, pointed out that it was extremely dangerous medicolegally to turn a private patient over to a resident without the patient's permission. If you are scrubbed, I see no reason why the resident could not perform the delivery and repair. We split up the cases so that somebody did the forceps, somebody else did the manual removal of the placenta, and, as the training proceeded, somebody else would repair the episiotomy. So, even if you do not have a large service, I think you can train a certain number of residents. Since 1931 we have finished only two residents a year, and we are running around 4,000 deliveries a year, so it shows you that we do try to give these men adequate material.

Regarding Dr. Russell's question, our study was made, but as far as I know, it has never been reported. There are four reports in the literature, one from the Chicago Maternity Center, with results similar to the others, which show that prolonged labor and forceps delivery, and difficult forceps delivery are accompanied by an increased stillbirth rate. The babies who survived were studied two to thirteen years later, and they are in no worse condition than babies born by so-called spontaneous delivery. The worst thing that can happen for the baby is the precipitate delivery.

# FURTHER EXPERIENCES WITH DIRECT SKY BLUE IN THE IN VIVO STUDY OF GYNECIC LYMPHATICS\*

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New and refined methods for the study of the patterns of the lymphatic system are being constantly devised. Bennett and Shivas² have recently reported on lymphangiography in animals using ethyl iodostearate. Although the product is toxic, the animals and their lymphatic systems recover. We have continued to use hyaluronidase† and Direct Sky Blue† without any toxic or noxious aftermath. The techniques have been described in our previous reports³,⁴ on the uterus and ovaries. In these studies we demonstrated that there were preferred channels, and that secondary pathways became apparent when the primary ones were obstructed. In our patients and in the experimental animals‡ the uterosacral ligaments assumed greatest importance in the mechanism of bilateral spread. It was these ligaments which were involved with the peritoneal reflection of the rectosigmoid in spread to the lower gastrointestinal tract. We ended our last summary with the statement that we were unable at that time to produce uniform extension to the external iliac group of nodes, and that we hoped to report progress at this meeting.

Preceding further discussion, may I stress that Direct Sky Blue is a soluble sodium dye salt in a buffered solution. With hyaluronidase used as a preliminary injection to enhance the spread and dispersion of the dye through tissues, the dye was picked up by the perivascular lymphatics, and was seen in the adventitia and internal elastic layer of these vessels (Fig. 1). The spread of the dye might thus be considered as "vascular" in type. Being a true solute, the dye was unable to block lymphatics. It has been found, however, in phagocytes in rat lymph nodes.

Since the results of our previous studies seemed to indicate that the external iliac nodes were secondarily involved only after the primary paths had been blocked by disease, it seemed desirable to attempt to develop a technique which would stain the external iliac nodes in a routine fashion. The first trials consisted of injecting the round ligaments in their lateral third, and distal to ligature of the round and upper broad ligaments. Results were disappointing. The major portion of the dye collected in the obturator and hypogastric basins. Next we opened the sheath of the external iliac vessels, and made multiple small

<sup>\*</sup>Presented at the Twenty-second Annual Meeting of the Central Association of Obstetricians and Gynecologists, St. Louis, Mo., Oct. 7 to 9, 1954.

<sup>†</sup>Wydase brand of hyaluronidase and Direct Sky Blue was furnished through the courtesy of Wyeth Laboratories.

<sup>‡</sup>Dogs were operated upon in the Katz-Sanders Laboratory for Experimental Surgery.

injections of the Wydase-dye mixture according to the technique described by Weinberg and Greaney,<sup>5</sup> but the spread was so variable as to be of no clinical value. Frequently all tissues became deep blue. We then gave up on transabdominal injections, and transferred our efforts to finding a suitable external portal to the external iliac lymphatics.

Female dogs were injected with 0 to 75 turbidity reducing units of hyaluronidase followed by 1 ml. Direct Sky Blue solution, 1 to 96 hours preoperatively. Injections were made into the sacrosciatic notch into or along side of the sheath of the sciatic nerve, and into the femoral or inguinal canals, always on the right side. Operations done the day of the injection showed no retroperitoneal dye, whereas the para-aortic nodes were stained at operations done over 72 hours after the injection. No dye was visualized along the external iliacs, however. It was believed that anatomic differences between dogs and women might account for these failures (Figs. 2 and 3).



Fig. 1.—Low power, unstained frozen section from uterine wall showing parallel layers of dye in vessel walls (printed from original Kodachrome).

A rather typical pattern of the venous tree of the female pelvis and perineum is shown in Fig. 4, although the connecting links between the femoral, external, and internal iliacs, and between the external and internal pudendal vessels are not shown. Anson¹ devotes several pages to these variations in arterial patterns. Aware that these channels do exist, we injected the perineal body and vaginal fourchette of each member of a group of patients, using up to 3 ml. dye in each subject. In the absence of inflammatory disease, approximately 65 per cent of the injected women have demonstrated staining of the sheath of the external iliac veins on the side of the injection providing this was done at least 24 hours before the operation. Arterial sheaths have shown very little, if any, dye. Contralateral staining occurred in one patient with extensive inflammation on the injected side. The route of transfer was not discernible.

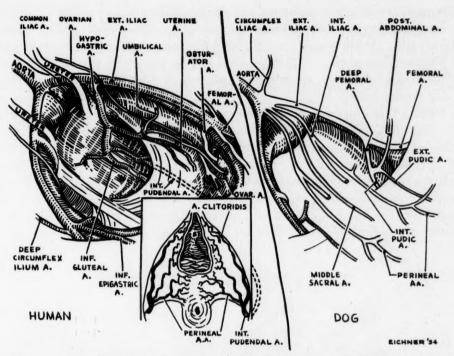


Fig. 2.—Schematic semioblique view of arterial supply in female human\* and dog† pelves. Note comparative terminations of aorta, and origins of internal iliac arteries. The dog's uteroovarian artery (not shown) arises near the kidney from the aorta to supply the ovary and uterine horn.

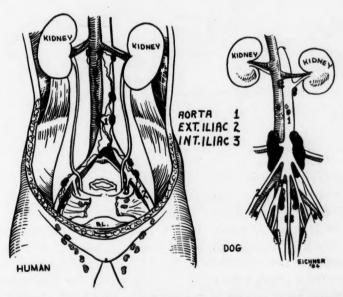


Fig. 3.—Schematic representation of comparable pelvic and aortic lymph node patterns in women\* and dogs.† Note the large conglomerate node lying at the distal end of the dog aorta, often called the "internal iliac" node. External iliac nodes are infrequent in the dog.

<sup>\*</sup>Modified and adapted from Smout and Jacoby: Gynecological and Obstetrical Anatomy and Functional Histology, ed. 3, Baltimore, 1954, Williams & Wilkins Company.

†After Merzdorf, in Sisson-Grossman: Anatomy of the Domestic Animals, ed. 4, Philadelphia, 1953, W. B. Saunders Company.

In the presence of pelvic inflammatory disease, sometimes of minimal character, dye remained invisible throughout the operation, apparently pooled near the injection site. At the end of the operation dye was often seen in the hypogastric and common iliac areas. Pathways could not be identified, and we were unable to state whether dissection opened new channels, or whether manipulation spread the dye mechanically.

During this study we never noted the transfer of visible dye to the inguinal area. Injections were made into various portions of the vagina, labium majus, frenum of the clitoris, and into the femoral canal. Femoral and inguinal canals were opened at operation done through Pfannenstiel incisions, and no dye was visualized, except in those patients whose injections were at the operative site. Injection into the femoral canal backed down the leg slightly, and then went mesially toward the labium and the pudendal basin (Fig. 5). This spread is probably through connections between the external and internal pudendal systems.

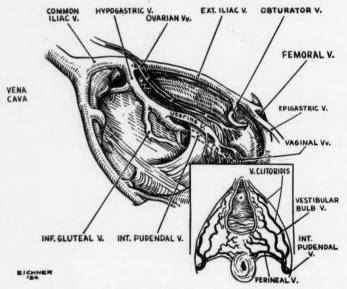


Fig. 4.—Schematic, semioblique view of the venous drainage of the human female pelvis.

Vulvovaginal injections primarily produced anterior spread. There was minimal posterior diffusion. Injections of the vagina and fourchette spread under and through the labia minora to the ipsolateral labium majus, occasionally spreading a little more laterally to the inner portion of the corresponding crural fold. Staining usually circled the clitoris, but did not stain the glans. The dye spread over the symphysis on to the anterior abdominal wall (Fig. 6). No injections of the glans were made. At operation dye was visualized in the deep subcutaneous tissues anterior to the rectus sheath. It occasionally crossed the midline in the area behind the symphysis, but remained anterior to the space of Retzius. Maximal spread was on the injected side, and, with a "clean" pelvis, the external iliac nodes and the adventitia of the vein were stained. Experimental work in dogs suggested that canine equivalents of the inferior epigastric

and circumflex iliac vessels in human beings constituted the major pathway to the external iliac basin. If the vulvovaginal injection was done deeply, the labial spread might be as described, but there would be a minimum of anterior abdominal dye. The greatest portion entered the pelvis through pararectal channels, but dye was seen in the obturator, hypogastric, and external iliac areas. Failure of dye to stain the labia minora and the inguinal area again emphasized the primary spread toward major collecting channels and nodal areas.

Fig. 5.

Fig. 6.

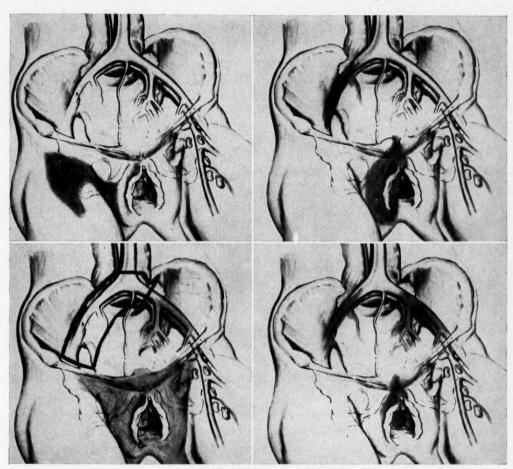


Fig. 7.

Fig. 8

Fig. 5.—Composite view of results of injections into the right femoral canal. Smudge represents skin spread of dye toward labium; dye also distally from point of injection (o). No dye reached external iliac vessels in 48 hours.

Fig. 6.—Composite view of results of injection (o) at fourchette. This represents labial or vulvovaginal injection as well. Labia minora were unstained. Labium majus showed maximal stain which spread anteriorly over symphysis. Smudge represents visible stain in vulvovaginal area, and along the external iliac vessels. Inguinal region unstained.

Fig. 7.—Composite view of modification of dye spread after extraperitoneal removal of all perivascular lymphatics on the right side of the pelvis (portion within black box). Superficial spread is far greater than previously, and internal spread is contralateral. Compare this spread with that observed in Fig. 6. Although drawing is of human subject, the described procedure was done only in dogs.

Fig. 8.—Composite view of vaginal paraurethral injection (o). Labial spread was minimal; systemic spread was most rapid. External iliacs were frequently involved bilaterally.

With the recurring evidence that blockage of any type modifies the pattern of spread, we then attempted to force dye into the inguinal area. The adventitia and sheaths of all major vessels in the right half of the pelvis of a mature female dog were removed extraperitoneally from the iliac crest to the deepest pelvis, and from the inguinal ligament to and beyond the bifurcation of the aorta. Injection into the fourchette was made in a routine fashion one week later. Dye spread anteriorly, posteriorly, and laterally far beyond that seen in any previous injection (Fig. 7). At operation five days later, dye had spread to the left external iliacs, but the side previously operated upon was free. Dye approached the inguinal area, but did not stain any nodes. This dog was not operated upon a third time, but approximately one week later the inguinal area showed blue stain for the first time. If interpretation of this result can be transferred to women, it suggests that complete lymphatic obstruction plus a prolonged interval of time is necessary before inguinal nodes can demonstrate vulvar disease.

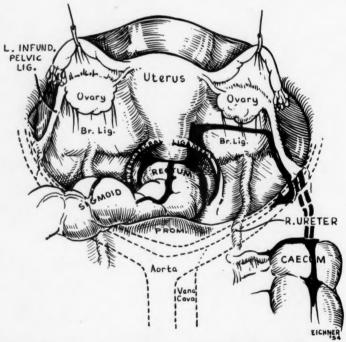


Fig. 9.—Schematic view of one of the unusual results of posterior injection in the inner third of the vagina. There was no anterior spread, and the teniae of the sigmoid and cecum as well as the right hypogastric nodes showed the presence of dye. The uterosacral ligaments and the cul-de-sac were also stained.

Injections done paraurethrally into the anterior vaginal wall usually spread bilaterally into the deep pelvis with a minimal spread to and through the labia as previously described. External iliac nodes were often involved bilaterally (Fig. 8). Systemic spread occurred frequently and early with this type of injection. Posterior injections of the distal vagina gave results similar to that of cervical injection. In one patient, however, the teniae of the sigmoid and cecum were beautifully stained. The external iliacs were free, but the hypogastrics were not (Fig. 9).

Dye often remained in the vulvovaginal areas at the injection sites for over six to eight weeks, yet never appeared to stain the inguinal region. Systemic staining occurred in several patients. In each case the neck and face appeared ashen gray one to two days before the shoulders and upper torso became colored. In general, the forearms and hands were unstained. Depending on the amount of dye adsorbed, each patient regained her normal tints in ten days to four weeks. The diagnosis of systemic spread can be readily verified by withdrawing venous blood, oxalated or otherwise. Serum and plasma will vary in color from royal blue to a pale chartreuse, depending on the amount of dye present. Blood will continue to fade toward the green to yellow shades at a relatively constant rate in vivo and in vitro. Except for appearances there were no adverse effects on any patient. The earliest systemic effect occurred within twelve hours after injection; the most delayed took three days. In two subjects operative manipulation produced the spread which became visible while the patient was still in the recovery room. The only changes in pulse, respiration, and blood pressure which occurred took place in the nursing personnel when these patients developed "acute cyanosis."

#### Summary

By using Wydase and Direct Sky Blue by injection on women and dogs according to techniques previously described, efforts were made to identify the preferred pathway for routine staining of the external iliac nodes. At the same time, the lymphatic drainage of the vagina, labia, femoral and inguinal canals was studied. Drawings made from Kodachrome transparencies taken at operation, and from operative notes, are presented and discussed.

# Conclusions

- 1. The preferred route for transmission of dye substances such as Direct Sky Blue to the external iliac nodal area is by injection of the fourchette or the labium majus.
- 2. Labial and vulvar drainage does not go directly into the inguinal nodes, but apparently follows the internal and external pudendal basins with their many variations.
- 3. Dye spread appears to be primarily by perivascular lymphatics, and by the internal elastic layer of the smaller vessels. This suggests that complete, curative surgery must remove the vascular sheaths of the regional arteries and veins. Dye has been seen in phagocytes in lymph nodes.
- 4. Results of stripping perivascular lymphatics in the dog suggest that extensive lymphatic blockage plus a variable but prolonged time interval is necessary for spread from the labia to the inguinal nodes.
- 5. Minimal degrees of pelvic inflammation or disease will modify or inhibit the pattern of "normal" dye spread.
- 6. Wydase produces greater dispersion of the dye, and is apparently necessary for adequate study of pelvic lymphatics. It is required in the older subjects, but may be dispensed with in some young, sexually active patients, particularly in early pregnancy.

7. Direct Sky Blue is an excellent and satisfactory tool for the study of "normal lymphatics," but does not appear to be the ideal agent for the study of pelvic lymphatics since its spread is modified or inhibited by all degrees of pelvic inflammation. It is this group of patients who require further study by techniques not yet in common use,6 or not yet devised.

We wish to express our appreciation to Mr. Robert Newhouse, assistant photographer at Mount Sinai Hospital, for his excellent cooperation and assistance, and to Henry Eichner of Los Angeles, brother of the senior author, to whom we are indebted for the drawings.

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#### Discussion

DR. EICHNER (Closing).-I will say that I am almost ready to give up this thing because minimal pelvic blockage stops the progress of the dye, and I was not able to get it where I wanted it to go.

In the systemic spread, this material apparently goes through the cisterna chyli and the thoracic duct into the neck, because the faces of these patients become blue (the torso does not) approximately three to five days later. The shoulders become grayish blue, but the hands do not.

In so far as the blockage of lymphatics is concerned, we are continuing this work experimentally on rats and smaller animals-dogs-to see how the dye is picked up. The material is deposited in the tissues and apparently settles there, finally, and phagocytes pick it up. The dye enters the lymph nodes from the circular channels on the periphery, and then traverses the nodes to the hilar area.

If these were cancer cells, I could understand why radioactive gold would hit some nodes, because until the entire periphery of that node is blocked, there are still some channels open to the hilus.

#### SITES OF METASTASES OF UTERINE CARCINOMA\*

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College of Medicine)

A NALYSIS of autopsied cases of uterine carcinoma has been made in order to determine the sites of metastases and mode of death. The effect of treatment upon the spread of the disease is the chief point of interest.

#### The Material

One hundred thirty-six cases are herein reported. There were 22 cases of endometrial carcinoma, 64 treated and 33 nontreated cases of cervical carcinoma, and 7 cases of uterine sarcoma.

The classification of the League of Nations has been utilized in determining the clinical extent of the disease during the hospital admission at the time of death.

The source of the material is the Gynecology Tumor Clinic, Ohio State University College of Medicine, and the Autopsy Protocol Library maintained by Dr. Emmerich von Haam, Chairman of the Department of Pathology, Ohio State University College of Medicine. Dr. von Haam and the Secretary of the Protocol Library, Miss Marian Snavely, have maintained the protocols on all autopsies performed in the City of Columbus since 1937. The protocols of 15,000 autopsies were searched to find the 136 cases herein reported.

The Gynecology Tumor Clinic is now maintaining records on 960 cases. Of these 960 cases, only one is untraced. Follow-up has been maintained on these cases dating back to June, 1940, and continuing up to January, 1954.

The format and figures in this article were adapted from Henriksen.<sup>1</sup> It is felt that the uniformity of reporting similar series will ultimately aid in a more valid statistical analysis.

## The Lymphatics of the Cervix (Fig. 1)

The lymphatic vessels and lymph nodes of the uterus are demonstrated in Fig. 1. Henriksen¹ separated the lymphatic nodes into primary and secondary groups.

I. The Primary Group.—

A. The Parametrium: The presence of small lymph nodes along the major lymphatic trunks transversing the parametrium is constant enough to permit their inclusion as a separate chain of lymph nodes.

B. The Paracervical (Ureteral) Node: Located near the crossing of the uterine artery and the ureter.

C. The Hypogastric Nodes: The uniformly small nodes in this group vary in number and location and are located along the course of the hypogastric vein near its injunction with the external iliac vein.

D. The Obturator Nodes: These are frequently described as one large node (Leveuf's node).

<sup>\*</sup>Presented at the Twenty-second Annual Meeting of the Central Association of Obstetricians and Gynecologists, St. Louis, Mo., Oct. 7 to 9, 1954.

E. The External Iliac Nodes: This group varies in number from three to eight nodes, which tend to be uniformly larger than the nodes of the other groups. Usually located in the sulcus between the external iliac artery and vein, they may be found entirely on the mesial surface of the vein.

II. The Secondary Group .-

A. The Sacral Nodes: This group includes the several nodes in the sacral concavity and on the sacral promontory.

B. The Common Iliac Nodes: These vary in number and location, but usually lie on the mesial and lateral surfaces of the common iliac vessels, just below the bifurcation of the aorta.

C. The Inguinal Nodes: These include the deep and superficial femoral

lymph nodes.

D. The Aortic (Periaortic) Nodes: These extend from the level of the bifurcation of the aorta to the diaphragm and they lie on the superior and lateral aspects of the aorta.

The lymph channels and node sites are often variable due to the ever-present intercommunicating subsidiary vessels and the relatively inconstant locations exhibited by some of the major nodes. It is not uncommon to find anomalous nodes along the lymph vessels connecting the major node groups. These intercommunicating vessels account for the unpredictable sites of some of the metas tases.

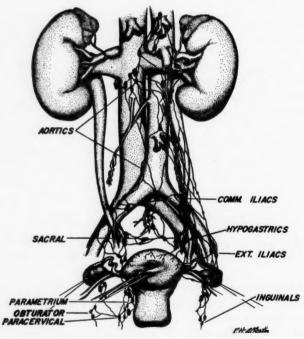


Fig. 1.—The lymphatic vessels and lymph nodes of the uterus.

The lymphatic vessels draining the cervix converge at the level of the junction of the cervix and the corpus to form the paracervical plexus, from which main trunks pass laterally, and follow the direction of the uterine veins. Between these main trunks are intercommunicating vessels, which permit the occasional by-passing of a major node group located along the main lymphatic route.

Channel 1: Arising from the paracervical plexus, and following the direction of the uterine artery, this channel connects with the paracervical, the external iliac, and the obturator nodes.

Channel 2: This channel also arises from the paracervical plexus, follows the course of the uterine vein posteriorly, to terminate in the hypogastric nodes. Intercommunicating vessels permit frequent metastases between the hypogastric, the obturator, the external iliac, and the sacral node group.

Channel 3: This is a smaller and less constant channel which passes forward and then backward along the uterosacral folds on both sides of the rectum, to terminate in the sacral nodes located in the concavity and on the promontory of the sacrum. Although this node group is included as a part of the secondary group of nodes, intercommunicating channels frequently permit metastases to the hypogastric nodes before the sacral nodes are involved. These subsidiary channels are so constant that it is permissible to interpret them as major routes.

### Part I

The incidence of node group involvement in cases of cervical carcinoma is divided into a treated and a nontreated series.

A. Carcinoma Cervix Uteri, 43 Nontreated Patients (Table I and Fig. 2).—Clinical Stage I, no cases.

Clinical Stage II, 2 cases: One patient had parametrial and paracervical node involvement. The other had hypogastric node metastases. The former died of a pulmonary embolus following a fractured hip at age 70.

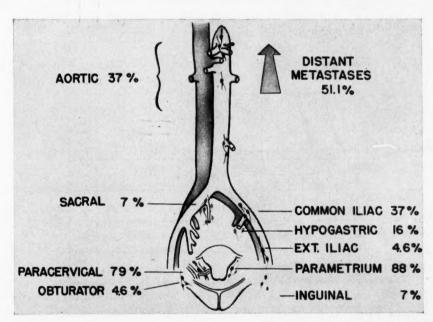


Fig. 2.—Incidence of node group involvement in 43 nontreated cases of cervical carcinoma.

The death of the other was caused by anesthesia during a radium implant at age 38.

Clinical Stage III, 5 cases: Primary nodes were found in all cases, secondary nodes in 3 cases, and distant metastases in 3 cases. One patient died of heart block, one of cerebral abscess, one in uremia due to obstruction of the ureters by tumor, one of uremia and hypertensive arteriosclerotic heart disease, and the last also in uremia due to carcinomatous obstruction of the ureters.

Clinical Stage IV, 36 cases: Thirty-five patients had primary nodes, 25 had secondary nodes, and 21 had distant metastases.

B. Carcinoma Cervix Uteri, 64 Treated Cases (Table II and Fig. 3) .-

Clinical Stage I, six cases: Two died of obstruction of the small bowel from radiation reaction with no evidence of residual carcinoma in the pelvis. Two died following the use of intra-arterial nitrogen mustard causing bowel necrosis. (A full report is in press.) One died of carcinoma of the pancreas with the cervical carcinoma cured. One died of coronary thrombosis. Node group involvement was absent in all cases.

TABLE I. INCIDENCE OF NODE GROUP INVOLVEMENT IN 43 NONTREATED CASES OF CERVICAL CARCINOMA.

	PARAM	PARAMETRIUM PARACERINGALS				OBTUB	SHOTA	HYPOC.	STAIC	Ext.	LIACS	COMME	W KACE	/NG/IIA.	STEAM	SACRAL	40ATICS	DISTANT METAST
	RT	LT.	RT.	LT.	RT.	LT.	RT.	LT.	RT.	LT.	RT.	LT.	RT	LT.				
STAGE I (0)	-	-	_	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
STAGE II (2)	1	1	1	1	-	-	1	1	-	-	-	-	-	_	_	_	-	
STAGE III (5)	5	5	4	5	1	1	-	-	-	-	1	2	-	-	1	1	1	
STAGE IV (36)	32	31	29	29	1	1	6	6	2	2	13	15	3	3	2	15	17	

TABLE II. INCIDENCE OF NODE GROUP INVOLVEMENT IN 64 TREATED CASES OF CERVICAL CARCINOMA.

	PARAMETRIUM		PARACEBUL	NICALS	OBTURATO	SHO	MPOGAC	THIC	EXT. ILIA	Source	COMMON	LIACS	INGUINALS	9	SACRAL	AORTICS	DISTANT METASTASE
	RT.	LT.	RT.	LT.	RT.	LT.	RT.	LT.	RT.	LT	RT	LT.	RT.	LT			
STAGE I (6)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
STAGE II (3)	2	2	2	2	_	-	-	-	-	-	-	-	-	-	-	-	i
STAGE III (2)	2	2	2	2	_	-	_	-	-	-	1	1	-	-	1	1	-
STAGE IV (53)	39	38	39	39	-	_	10	11	1	1	17	14	-	-	1	11	36

Clinical Stage II, 3 cases: One patient had obstruction of the ureters from tumor tissue with primary node involvement. This patient died in uremia. One patient, who died in diabetic acidosis, had primary group node involvement. One patient died from perforation of the ileum from irradiation reaction with no evidence of residual earcinoma.

Clinical Stage III, 2 cases: One patient died following an auto accident in which she suffered multiple rib fractures and had a massive pulmonary embolus. Both primary and secondary nodes were involved. The other patient died in uremia because of ureteral obstruction due to primary and secondary node group involvement.

Clinical Stage IV, 53 cases: Forty-three patients had primary nodes involved. Thirty-one had involvement of secondary nodes and there were 37 with distant metastases.

# Node Involvement (Table III) .--

Primary nodes were involved in 73.2 per cent of the treated cases and 95.2 per cent of the nontreated cases. Secondary nodes were involved in 48.4 per cent of the treated cases and in 65.0 per cent of the nontreated cases. This indicates that irradiation did destroy the immediate adjacent nodes in a significant number of cases. The reverse is true in the distant metastases. There were 11.6 per cent more distant metastases in the treated group than in the nontreated group.

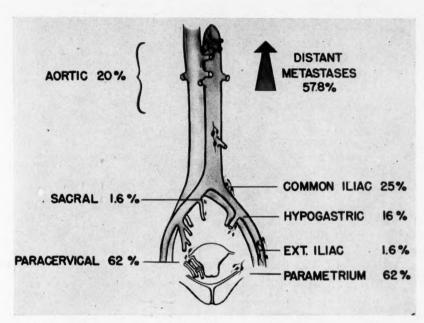


Fig. 3.—Incidence of node group involvement in 64 treated cases of cervical carcinoma.

# Distant Metastases in Cervical Carcinoma (Figs. 4 and 5) .-

It was formerly taught that syphilis is the mimic of all diseases. We would like to suggest that carcinoma be named to this nonenviable role for surely it can involve any organ. This is borne out by the review of the sites of distant metastases in the autopsied cases.

Specifically, it should be pointed out that there is a high incidence of pulmonary tract involvement. The pleura and lungs were involved in 12.5 per cent of the treated cervical carcinoma cases and in 23.2 per cent of the nontreated cases. The liver was involved in 23.4 per cent of the treated and in 32.6 per cent of the nontreated cases. In scanning Figs. 4 and 5, one sees that no system is immune from attack. Spread by the lymphatic channels alone cannot explain the widespread metastases. The hematogenous route is obviously also used. Of particular interest is the spread to the brain in 2 cases, to the heart in 5 instances, to the adrenals in 6 cases, to Virchow's node, the left supraclavicular node usually mentioned as a common site of metastases of cancer of the stomach, in 3 cases. The vertebrae were involved in 5 cases, the ribs in 4 cases, and pelvic bone in one case. With respect to bone involvement, we feel certain that many metastatic sites are overlooked. We have instituted the policy of taking over-all bone x-rays on the terminal patients. Thus we can utilize the roentgen findings at the time of autopsy to ensure proper localization of bone metastases.

#### Fistulas -

With regard to rectovaginal fistulas and vesicovaginal fistulas, there were more in the treated group, percentagewise. Of the treated cervical carcinoma

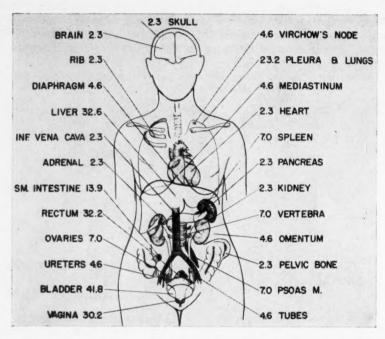


Fig. 4.—Incidence of distant metastases in 43 nontreated cases of cervical carcinoma.

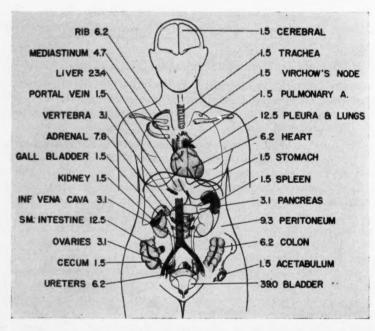


Fig. 5.—Incidence of distant metastases in 64 treated cases of cervical carcinoma.

group, there were 8, or 12.6 per cent, rectovaginal fistulas and nine, or 14.1 per cent, vesicovaginal fistulas. In the nontreated group there were 3, or 6.9 per cent, rectovaginal fistulas and 7, or 16.4 per cent, vesicovaginal fistulas.

TABLE III. INCIDENCE OF NODE GROUP INVOLVEMENT IN 107 TREATED AND NONTREATED CASES OF CERVICAL CARCINOMA.

STAGE	PRIMARY	SECOND.	DISTANT
	NODES %	NODES %	METAST. %
I TREATED NON-TREAT.	-	=	_
TREATED NON-TREAT.	3 4.6	=	=
TREATED NON-TREAT	1.5 9.3	6.9	2.3
TREATED NON-TREAT	68.7	48.4	57.8
	81.3	58.1	48.8
TOTAL	732	48.4	57.8
NON-TREAT	952	65.0	51.1

TABLE IV. INCIDENCE OF NODE GROUP INVOLVEMENT IN 22 CASES OF ENDOMETRIAL CARCINOMA.

	PARA	THUM!	PARACERICALS		PARACENICAL		08716	SHOW	HYPOC	STRIC	Bri	SOM	COMMO	NA ILIACS	/NG/III	STANIE	SACRAL	40RTIC	METAST
STAGE	IK!	LI	RT.	U.	RT.	LT.	RT.	LT,	RT.	LI	RT.	LT.	RT,	LT,		-			
I	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
STAGE II (0)	_	_	-	-	-	1.	_	-	-	-	_	_	-	_	_	_	-		
STAGE III (I)	1	1	1	1	-	-	_	-	-	-	1	-	-	-	_	1	1		
STAGE	12	12	12	12	-	-	_	-	-	-	3	4	1	1	_	7	16		

# The Assigned Cause of Death in Cervical Carcinoma.—

Uremia is the recognized major cause of death in cervical carcinoma, and so it was in our series. It was listed as the major cause of death in 36 cases, or 33.6 per cent. It was given, however, as a contributing factor in an additional 14 cases for a total, therefore, of 46.7 per cent of the cases. Carcinomatosis or cachexia was given as the cause of death in 25, or 23.3 per cent, of the cases. Peritonitis or bowel obstruction was found in 16 cases. Fourteen other patients died from the following causes: two, septicemia; one, cerebral hemorrhage; one, cerebral hemorrhage from metastases; one, cerebral hemorrhage post prefrontal leukotomy; one, post craniotomy for cerebral metastases; two, pulmonary emboli; one, diabetic acidosis; one, ruptured cerebral aneurysm; one, anesthetic, and one, pemphigus.

#### Part II

The incidence of node group involvement in cases of endometrial carcinoma is as follows (Table IV and Fig. 6):

A. Treated Endometrial Carcinoma, 13 Cases.— Clinical Stage I and II, no cases. Clinical Stage III, one case: Paracervical, parametrial, common iliac, and aortic node involvement. Death was due to postoperative pulmonary embolus at the time of hysterectomy.

Clinical Stage IV, 12 cases: Paracervical and parametrial nodes were involved in 5 cases, common iliac in 2, aortics in 3, and there were 9 cases of distant metastases.

B. Nontreated Endometrial Carcinoma, 9 cases .-

Clinical Stages I, II, and III, no cases.

Clinical Stage IV, 9 cases: Parametrial and paracervical glands were involved in 7 cases, common iliacs in 2 cases, inguinal nodes in one case, aortic nodes in 4 cases, and distant metastases were found in 7 cases.

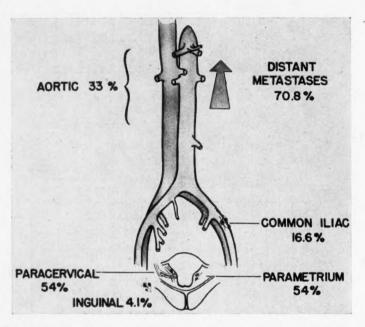


Fig. 6.-Incidence of node group involvement in 22 cases of endometrial carcinoma.

Distant Metastases in Endometrial Carcinoma (Fig. 7).—

The lungs were the site of metastases in 33.3 per cent of the cases of endometrial carcinoma. The liver was involved in 31.8 per cent of the cases. The omentum was involved in 22.7 per cent of the cases. All systems showed metastatic sites. Of interest in two cases was the spread to the trachea causing death by asphyxia in one of these cases. Reference to Fig. 7 will show the multiple sites of metastases. No rectovaginal or vesicovaginal fistulas were found.

The Assigned Cause of Death in Endometrial Carcinoma.

Carcinomatosis associated with some intercurrent infection such as pneumonia is the major cause of death in endometrial carcinoma. Ten of the 22 patients, or 45.4 per cent, died because of carcinomatosis; 4, or 18.2 per cent, died of bowel obstruction or peritonitis; one of hemorrhage; one of tracheal asphyxia from metastases; one of brain metastases; one of periarteritis nodosa; one of postoperative pulmonary embolus; one of hypertensive heart disease; one of perinephric abscess, and one of uremia secondary to ureteral obstruction.

#### Part III

Sites of Metastases of Uterine Sarcoma.—

Seven patients with sarcoma of the uterus came to autopsy. The most striking finding is the number and size of metastases. The theory that sarcoma spreads by the blood stream is borne out by the overwhelming number of organs listed in the individual cases. All cases had primary node involvement. The paracervical and parametrial glands were involved in every instance. Other sites of metastases, recorded by case, were:

Case 1: Secondary nodes, including the iliacs and aortic nodes. Also involved were the lungs, ileum, appendix, and rectum.

Case 2: Secondary nodes, including the iliacs and aortic. Listed as sites of metastases were the lungs and pleura, pericardium, endocardium, pulmonary artery, liver, kidneys, adrenals, pancreas, peritoneum, intestine, skin, and Virchow's node.

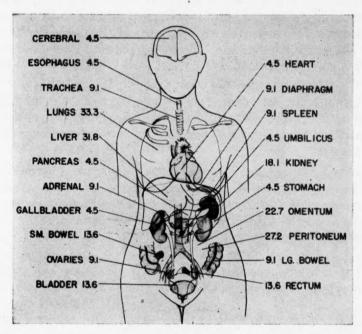


Fig. 7.—Incidence of distant metastases in 22 cases of endometrial carcinoma.

Case 3: All pelvic node categories showed involvement. The lungs, diaphragm, liver, parietal peritoneum, and intestines showed metastases.

Case 4: All pelvic node categories showed involvement. The left tube and ovary, aortic nodes, suprapancreatic nodes, pancreas, spleen, adrenals, and liver were sites of metastases.

Case 5: This case had only primary node involvement; the sarcoma, however, had perforated the uterus which measured 20 by 20 by 8 cm. The patient was 72 years old and died of a pulmonary embolus. No tumor cells were found in the embolus.

Case 6: The primary nodes were involved. Also found as metastatic sites were the ileum, colon, liver, right tube and ovary, bladder, and rectum.

Case 7: The pelvic nodes were all involved. Other sites of metastases were the kidneys, adrenals, mesenteric nodes, pancreatic nodes, diaphragm, liver, gall bladder, spleen, omentum, lungs and pleura, colon, aortic nodes, mediastinal nodes, and the thyroid.

The Assigned Cause of Death in Uterine Sarcoma .-

Carcinomatosis was given as the cause of death in 4 of the 7 cases. One patient died of a pulmonary embolus, one in uremia due to ureteral obstruction, and one from peritonitis following complete bowel obstruction.

# Summary

The sites of metastases of 136 cases of uterine carcinoma have been indicated in graphic form. The spread to primary and secondary node groups has been broken down to specific anatomic sites. In addition, the spread of carcinoma to distant sites of metastases has been analyzed in 64 treated cases of cervical carcinoma as compared with 43 nontreated cases of carcinoma.

Significant is the relationship of treatment to the spread of carcinoma. In the treated cases the primary nodes were involved in 73.2 per cent of the cases as compared with a 95.2 per cent involvement in the untreated cases. The secondary nodes were involved in 48.4 per cent of the treated cases and in 65.0 per cent of the nontreated cases. This would indicate local destruction of the carcinoma in a significant number of treated cases. When death ensued in these same cases, there were more distant metastases in the treated group than in the nontreated group. The incidence of metastases was 57.8 per cent in the treated, as compared with 51.1 per cent in the nontreated. This bears out the fact that therapy can destroy local growth, but the untreated distant metastases go on to kill the host.

The assigned cause of death in cervical carcinoma was directly due to carcinoma in 88 per cent of the 107 cases. In the cases of endometrial carcinoma, death was attributable to carcinoma in 18 of the 22 cases. In the 7 cases of uterine sarcoma, 6 of the 7 deaths were caused by tumor growth. The remaining 24 of the 136 patients died of causes other than carcinoma. The diagnosis of carcinoma should not mislead the clinician into overlooking other disease entities in the individual patient. Conversely, carcinoma can simulate many other disease types.

#### Reference

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# Discussion

DR. JOHN A. WALL, Houston, Texas.—The incidence of node group involvement in these 64 treated cases has been compared to that in 43 untreated patients and it illustrates diminution in node involvement in those patients subjected to therapy. The increase in generalized metastases in the treated group serves to prove the local disease can frequently be arrested. Morton demonstrated the serious effect on prognosis exercised by regional lymph node metastasis in a study of 409 deaths from carcinoma of the cervix. He pointed out that death from distant metastasis frequently followed complete control of local disease. The ability to control local disease, it seems to me, is testimony to the fact that one of the current responsibilities of clinicians is to establish an early diagnosis in carcinoma of the cervix.

These cases here presented do not represent an effort on the part of the authors to evaluate the therapy to which they were subjected. The material is not only from the Gynecological Tumor Clinic of the Ohio State University College of Medicine, but also autopsies performed in the city of Columbus since 1937. Therefore, it is important that this report should not be misconstrued as a detailed evaluation of therapy. This cannot be done be-

cause, for example, these individuals were classified according to the clinical stage of advance at the time of their terminal hospital stay. One cannot stage carcinoma of the cervix after therapy has once been instituted. Henriksen and Morton, in contrast to the material of the present authors, employed the clinical stage of the disease before the institution of therapy in evaluating their results. Morton, on the other hand, is the only one of these three who has correlated the treatment administered with the autopsy findings.

The authors have studied the autopsies in adenocarcinoma of the endometrium and there is in this treatise verification of the generally held clinical impression that there is a decreased incidence of death from endometrial carcinoma as compared with cervical carcinoma. There were, for example, only 22 patients with endometrial cancer whose autopsy protocols were available for study. There was node involvement only in the cases of very advanced neoplasms. Twenty-two patients is too small a number to be of statistical significance and, furthermore, these patients were not separated into those with the disease limited to the fundus and into those with extension into the cervix (corpus et colli). Carcinoma of the endometrium with extention to the cervix is an entirely different clinical problem from a malignancy confined to the corpus. Corpus et colli lesions have a much higher incidence of lymph node metastasis because of the lymph drainage of the cervix.

Sarcoma of the uterus has been highly fatal in all clinics and the organs involved in the patients presented by Holzaepfel and Ezell would certainly indicate the probability of spread by the blood stream. We look on sarcoma of the uterus as a neoplasm which has to be treated primarily by surgery in all instances and endeavor to carry out radical lymphadenectomy as well as a radical hysterectomy.

I cannot resist the temptation to point out some of the possibilities for prevention of death from carcinoma of the cervix. We know that this neoplasm tends to remain localized in the cervix and paracervical areas for quite a long time. Adequate treatment of the primary lesion in the cervix and the immediately adjacent paracervical triangle should be successful where the disease is early. Success in treatment of carcinoma of the cervix depends upon the volume of tumor. This applies equally whether one chooses surgical excision of the disease or sterilization by some form of irradiation. We have come to look upon local recurrence as manifestation of inadequate dosage. We are now in the process of repeating what has been done previously, namely, serial biopsies during and following treatment. This effort is being made to demonstrate that the local disease, regardless of the clinical stage, can usually be obliterated provided the cancerocidal dose can be delivered to the surface of the tumor. This does not mean, however, that tumor which has extended beyond the paracervical triangle can be destroyed by the same dosage which will sterilize a much smaller total volume of tumor confined to the cervix any more than one can surgically remove a big mass of tumor as adequately as one which is limited to the cervix.

Supervoltage therapy does offer possibilities to patients over 20 cm, thick as well as those in whom dosages up to 5,000 r are considered necessary for complete obliteration of disease which has extended beyond the cervix. We are now doing lymphadenectomies in selected patients in clinical Stage II and Stage III after parametrial external irradiation. We have recently studied a patient with clinical Stage II carcinoma of the cervix who had palpable evidence of metastatic cancer in the left obturator lymph node prior to the institution of therapy. She received 1,500 gamma roentgens from radium to each pelvic wall and in addition by means of external irradiation delivered by the cobalteo irradiator, 3,000 r to the right parametrium and 5,100 r to the left parametrium. Degenerating squamous-cell carcinoma was demonstrated histologically in the center of the node removed after completion of radiotherapy. We feel this is positive proof that metastatic squamous-cell carcinoma can be destroyed in the regional lymph nodes.

DR. JOHN I. BREWER, Chicago, Ill.—I wish the essayist would tell us a little of the management of the patients and a little about their end results.

DR. HOLZAEPFEL (closing).—The method of treatment currently used is as follows: We use a cobalt applicator which delivers at point "A" 5,500 r, and 1,300 r at point

"B." The cervix or the tumor area receives this 25,000 r; the lateral vaginal wall receives 15,000 r. We use external therapy designed to deliver 4,000 r at point "A" in the midpelvis. We deliver 4,000 r to the midpoint. The total irradiation can be summarized: 9,500 r to point "A," 5,300 to point "B," 29,000 r to the cervix, of course, used only because we have the screening area and the thickness of the cervix, 19,000 r to the lateral vaginal wall.

The absolute five-year survival rate is as follows:

At clinical Stage Zero, 25 patients, 96 per cent; clinical Stage I, 87 patients, 72 per cent; clinical Stage II, 166 patients, 45.9 per cent; clinical Stage III, 210 patients, 28.6 per cent; clinical Stage IV, 82 patients, 0.0 per cent. The total absolute survival is 44.5 per cent in cases of cervical carcinoma.

In the endometrial carcinoma cases the absolute five-year survival is 67.3 per cent.

We are most proud to report that of the 1,056 cases of pelvic cancer under our surveillance there are no lost patients, there are no untraced patients.

# A BEAD PACKING TECHNIQUE FOR THE APPLICATION OF UNIFORM DOSES OF IRRADIATION TO THE ENDOMETRIAL CAVITY\*

# An Experimental Approach

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THE most effective currently available therapeutic approach to the problem of endometrial carcinoma, according to most workers in this field, is the combination of some form of irradiation with subsequent hysterectomy.

Carcinoma of the endometrium remains essentially a surface lesion during the time when it is most amenable to cure. It is impossible, by definition, to determine other than in retrospect most of those cases in which the lesion has already metastasized at the time of initial therapy. From 5 to 10 per cent of cases, for example, are estimated to have nonpalpable tubal and/or ovarian metastasis at the time the diagnosis was made,¹ and the finding at laparotomy of even more distant unsuspected spread is a discouragingly common experience. In view of the fact that such cases cannot all be diagnosed prior to treatment, and in view of the limited effectiveness of the combined irradiation-surgery therapy, the corrected survivorship of that group of patients originally considered to have a favorable prognosis will always be less than 100 per cent until a more specific form of therapy can be devised. In the absence of palpable evidence of extension, however, each individual case must be managed on the assumption that it is curable.

While it has not been claimed that eradication of all tumor cells in the uterus is one of the principal goals in the management of endometrial cancer (inasmuch as the primary lesion is to be removed later), it is assumed that the degree to which tumor can be eradicated in the uterus prior to its removal does have at least some pertinent bearing on the five-year survivorship. Arneson and associates<sup>2</sup> and Taylor and Becker<sup>3</sup> had a significantly higher percentage of five-year survivors in cases where there was no residual tumor identified in the uterus which had been removed after preoperative radium therapy than they had in cases where the uterus contained residual carcinoma. As methods of wider dispersal of intrauterine radiation sources have become available, there are an increasing number of reports in the literature of surprisingly lowered percentages of residual carcinoma in operative specimens. Following the use of "Y" applicator and preliminary roentgen therapy,

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<sup>\*</sup>Presented at the Twenty-second Annual Meeting of the Central Association of Obstetricians and Gynecologists, St. Louis, Mo., Oct. 7 to 9, 1954.

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Schmitz, Sheehan, and Towne<sup>4</sup> found tumor cells remaining in only 16.5 per cent of the uteri examined from one series. Using the hysterostat, Friedman<sup>5</sup> had only 12.5 per cent residual carcinoma, but in a subsequent series by the same technique<sup>6</sup> there was residual tumor in 85 per cent of the uteri. Using the packing method, Arneson, Stanbro, and Nolan<sup>2</sup> had 26.3 per cent specimens with residual carcinoma.

It is felt that the degree to which multiple weak sources of radioactive material can be widely and homogeneously distributed throughout the uterine cavity is probably the most important criterion of potential success in the irradiation phase of the management of endometrial carcinoma. Thus uniformity of distribution rather than total cell necrosis alone should be stressed for maximum results.

If sufficient radiation can be administered to cause cytologic and histologic changes incompatible with metastasis, all the residual "sickened" cells will be removed at the time of hysterectomy anyway, before any remaining tumor becomes reactivated. Supporting the contention that total necrosis of the neoplastic cells is not a prerequisite for successful therapy are the excellent survivorship figures of Scheffey, who, in a selected series of patients treated by radium followed by hysterectomy, reported a 91 per cent five-year survivorship; in spite of the exceedingly high rate of patient survivorship, 52 per cent of the excised uteri showed residual carcinoma!

The utilization of high dosages, on the other hand, is accompanied by two dangers: (a) the peripheral danger of excessive damage to bowel and bladder, and (b) the central danger of massive necrosis of normal tissue to a point where a "supralethal reaction" is produced, allowing any remaining viable tumor cells to proliferate rapidly.

Granting, then, that some form of intrauterine radiation constitutes a part of today's therapy of choice, such an application should be made as effective as possible while at the same time the radiation of surrounding nonuterine tissue is kept at a minimum. Any improvement in current methods of therapy should provide for an effective dosage to the entire endometrial surface, while at the same time ease of application is maintained and undue exposure to the operator avoided.

The present report concerns the development of an experimental method, rather than the presentation of a series of treated cases. In the hope of making available an improved form of therapy, a technique has been refined to provide for the more uniform application of multiple small sources of radioactive material to the uterine cavity. The method which has evolved utilizes small metal spheres containing cobalt<sup>60</sup> threaded on strong sutures (like strings of beads). Such an assembly facilitates ease of insertion and removal and increases the uniformity of the packing distribution. This study is unique in that specific provisions have been made for individualization regardless of uterine size, with minimal exposure of the operator to radioactivity during the application. This method has been worked out entirely independently of a similar technique recently reported by Becker and Scheer.<sup>9</sup>

# Equipment

Stainless steel spheres \(^{5}\)<sub>16</sub> inch in diameter are used. After axial holes are bored, a small hollow cylinder of Haynes alloy 25 is fitted into the bore, as shown in the inset of Fig. 1. Haynes alloy 25, containing 50 per cent cobalt<sup>60</sup>, has the property of being resistant to fragmentation. The fitted spheres are then plated with nickel by the Kanigen process to ensure against oxidation. The beads are strung into chain form (Fig. 1) in varying lengths containing 10, 15, 25, and 35 beads, respectively. These chains of spheres may then be used either singly or in combination to the capacity of any uterine cavity as long as the loading of the beads of the various chains remains uniform. The chains of each length are prepared in pairs: an "active" chain, in which the beads are loaded with cobalt<sup>60</sup> sources and a "dummy" chain of inert beads which are used for determining the proper length of chain which will fill any given uterine cavity.

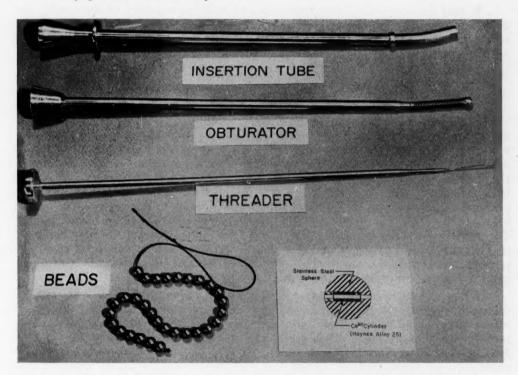


Fig. 1.—A "bead chain," together with the component parts of the bead insertion equipment. Inset shows the arrangement of the small cylinder of cobalt-containing Haynes alloy 25.

For packing the beads into the uterus, a "bead loader" was designed (Fig. 1). This consists of a straight % inch outside diameter stainless steel tube, one end of which is gently curved. The curved portion is inserted directly into the cervical canal. To increase the ease of passing the tube into the cervical canal, an obturator is inserted into the tube with its rounded end projecting smoothly. A stainless steel spring just behind the end of the obturator allows it to adjust to the curved portion of the tube.

### Technique of Application

The uterine fundus is sounded and the cervical canal is gently dilated until the insertion tube, with obturator in place, may be introduced smoothly

just beyond the level of the internal os (Fig. 2A). The obturator is then withdrawn for test loading. A string of dummy beads is selected for testing the capacity of the uterus. The average-sized uterine cavity has been found to hold 15 to 35 spheres. The end of the string is then drawn through the obturator by the use of the special threader (Fig. 2B), until the chain of spheres is fixed tightly to the distal end of the obturator. The beads are then allowed to feed down by gravity into the insertion tube. Gentle pressure on the obturator is used to pack the uterine cavity to capacity with dummy spheres (Fig. 2C). If mild resistance is encountered, a slight rotation of the axis of the tube will often permit more beads to be introduced without undue pressure. A length of beads is determined which will approximately fill the fundus and the cervical canal. The position of the most proximal bead on the chain may be judged with great accuracy by observing the distance the end of the obturator projects from the tube entrance.

It may be seen that, having thus determined the capacity of the uterus, the "dummy" chain may be removed and a "loaded" chain of the same length inserted in its place. Until the moment of actual insertion, the "loaded" chains are kept in sterile solution in a special protective lead container. Thus the actual time of exposure of the operator to radioactive sources is less than a minute.

# Study of the Technique

"Dummy" bead implantations were carried out immediately prior to operation in a series of 12 patients who were being operated upon for non-malignant gynecologic conditions. Figs. 3A and 3B show the even distribution of the beads through the uterine cavity in 2 such patients. It was found that the packing process could be readily accomplished once the cervical canal had been sufficiently dilated to allow for easy insertion of the tube. In some of these patients the beads were left in situ during the hysterectomy (the cervix having been sewed closed), in order that the placement might be studied more directly. The ability of the beads to adapt to an irregular uterine contour is well indicated in Fig. 4A, where a defect in the symmetry of the pattern was produced by a myoma encroaching on the lumen. Fig. 4B shows the adaptation of bead placement to changes in uterine contour produced by a myoma.

When it had been demonstrated that the beads could be inserted without difficulty into uteri of varying sizes and contours, the adequacy of the filling was evaluated by various methods and the accuracy of placement was compared with that of the tandem technique. These studies were carried out on 10 uteri just after they had been surgically removed. All the following studies were done on these surgical specimens: (1) After instillation of Lipiodol into the uterus, posteroanterior and lateral roentgenograms were made. (2) The uterine cavity was sounded and there was inserted a dummy steel rod of the proper length to simulate an individualized tandem application. Posteroanterior and lateral films were made of this placement. (3) The "tandem" was removed and the uterus packed with beads, after which further films were taken. (4) The uterus was incised and the beads photographed in situ.

In general, these studies indicate that the mass of beads closely approximates to the contour of the uterine cavity as indicated by Lipiodol; and that the relationship between the "tandem" and the uterine cavity leaves much to be desired. All these points are well illustrated by study of the illustrations from one of these cases, shown in Fig. 5. In Fig. 5,A the uterine cavity is outlined by the contrast medium, and a tandem has been slipped into place: there is marked deviation from the midline, in spite of the fact that an effort was made to obtain a central placement. Fig. 5,B shows the bead placement,

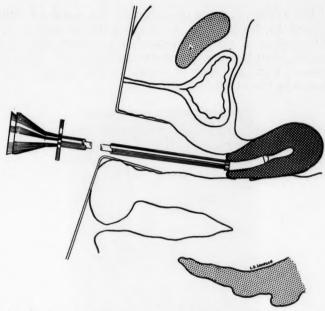


Fig. 2A.—The insertion tube, obturator in place, inserted into the dilated cervical canal just beyond the level of the internal os.

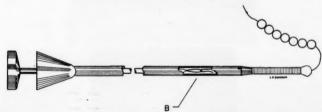


Fig. 2B.—Pulling the end of the bead chain up through the obturator with the threader. The end of the threader is shown at point B, with a loop of string threaded into it.

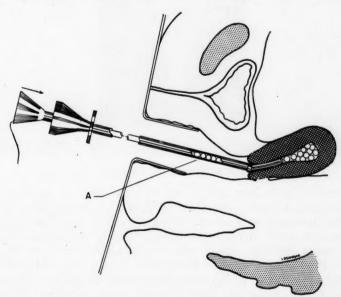


Fig. 2C.—Showing the uterine cavity partially packed with spheres.

with nearly all the available space occupied by the spheres. Superposition of the pattern formed by the spheres over the pattern formed by the tandem offers a good illustration of the inadequacy of a tandem type of treatment for endometrial lesions, even in cases where the tandem is of adequate length. In the last illustration, Fig. 5C, there is shown by photography the actual placement of the spheres in the uterine cavity.



Fig. 3A.—A 10 bead pack in place. Anterior view.

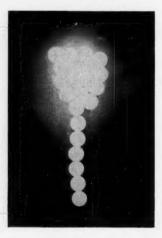


Fig. 3B.—Radiographic study of beads in situ. Lateral view.

### Formulation of Dosage

In the decision as to how best to achieve the aims of therapy with a packing technique (i.e., adequate surface endometrial irradiation without either massive central necrosis or damage to surrounding nonuterine structures), a number of factors need to be considered. Significant among these are: (1) The dosage range within which effective therapy may safely be applied. (2) The form of bead loading, and the size of beads. (3) The contour assumed by the packing material. (4) The number of individual sources in the volume pack.

These factors will be discussed sequentially.

1. Dosage Range Within Which Effective Therapy May Safely Be Applied.— Freed and Pendergrass<sup>10</sup> believe that adequate management can be effected when the dose to the outer wall of the uterus is within the range of 7,000 to 15,000 gamma roentgens (within a factor of 2.14), with the dose applied over a 2 to 3 week period. We believe that, while dosage within the range given does provide adequate irradiation, such high dosage is probably not a prerequisite for the successful management of endometrial carcinoma in those cases where the primary lesion is to be removed surgically soon after



Fig. 4A.—Bead placement adapted to irregular contours produced by fibroid.

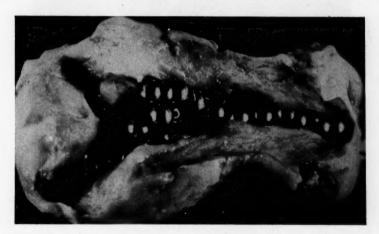


Fig. 4B.—Photograph showing adaptation of bead placement to changes in the uterine contour produced by fibroid.

irradiation. As Javert11 has said, "It is quite likely that the intracavity radium helps to localize the lymphatic and vascular cancer emboli in the uterus and prevent their dissemination during the surgical hysterectomy." The employment of irradiation to inhibit metastasis does not automatically imply that cancerocidal dosages are necessary or even desirable. This opinion is strengthened by the work of Heyman,12,13 where dosages as low as 1,800 r, supplemented by external x-ray therapy, have led to good results. Granting that, in the light of available information, this determination must remain somewhat empirical, it appears that adequate prehysterectomy preparation might be secured by irradiating the outer wall of the uterus, assumed to be 15 cm. from the endometrial surface, with dosages in the range of 2,500 to 4,500 r.

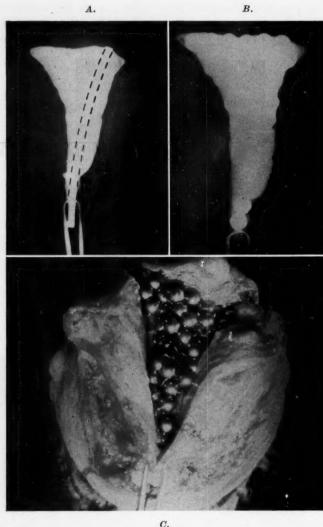


Fig. 5.-by Lipiodol. 5.-A, Tandem in place in a large adenomyomatous uterus. The cavity is outlined

B, The same uterine cavity packed with beads. Note the close approximation between the Lipiodol contour (A) and the bead contour shown here.

It may be pointed out that, while the proposed dosage range is significantly less than that which has theoretically been employed in many such schedules, it specifies a low ratio of maximum to minimum dosage of 1.8. This assumes a method of treatment with which practically uniform dosage is secured over the outer wall of the uterus. Such an assumption is invalid when a tandem is used for irradiation, for in this case necrotizing dosages are required centrally in order to attain even a modest amount of peripheral irradiation in some critical areas (i.e., cornual regions).

C, Photograph of the same uterus after it had been incised with the beads in situ.

# 2. Form of Bead Loading, and Size of Beads .-

One problem in securing adequate dosage to the outer wall of the uterus is the danger of delivering simultaneously necrotizing doses to the inner wall. The method of loading the beads has direct bearing on this problem.

Calculations indicate that an 0.8 cm. diameter bead (5/16 inch diameter) with cobalt uniformly distributed throughout its volume (i.e., cobalt alloy) will exhibit a 50 per cent higher dose rate on its surface than will a similar-sized bead loaded by concentrating all radioactivity at the center, when the activity of both beads is adjusted to give equal dose rates at 1.5 cm. from the center of the beads.

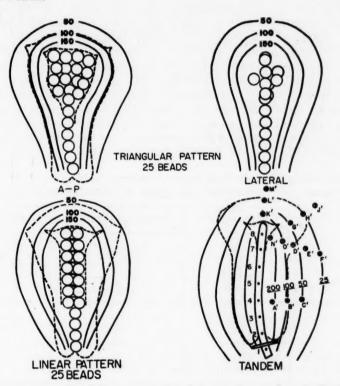


Fig. 6.—Showing the effect of varying the bead packing contour upon the maximum-to-minimum dosage ratio at the outer walls of the uterus. With a triangular pack, the ratio approximates 1.0. With the linear pattern shown here, the ratio would approximate 3.0. This compares with a ratio of 4.0 for an individualized tandem.

In a multiple bead loading pattern, uniformly loaded beads will exhibit surface dose rates approximately 30 per cent higher than similar patterns formed with centrally loaded beads, for equal dose rates 1.5 cm. from the surface.

Therefore, centrally loaded beads are the choice to satisfy clinical criteria for low surface-to-depth dose ratios. Much of this advantage would be lost were the beads to be smaller than suggested here.

No significant difference is found when comparing Lucite beads to stainless steel beads with regard to the surface-to-depth dose ratio. More source activity is required to compensate for the differential absorption increase of the stainless steel to secure the same dose rate as can be secured with the Lucite beads, but the susceptibility to radiation change of the Lucite offsets this advantage.

### 3. Contour Assumed by the Packing Material.—

The contour assumed by the beads will be variable, depending both on the configuration of the uterine cavity and on the amount of pressure used to pack the uterus. Alteration of the packing contour will, of course, alter the isodose curves. Volume packing may vary in extremes from a somewhat linear type of contour (in the uterus with a long narrow cavity) to more triangular or spherical contours (in uteri of greater fundal capacities). The ideal configuration in most cases approaches the triangular, since such a contour serves to keep the maximum-to-minimum ratio of dosage to the outer walls of the uterus as low as possible.

Using the bead packing technique, the dose ratio over the outer wall of the uterus can vary from a little less than 3.0 for a linear pattern down to an approach to the ideal 1.0 for a triangular pattern. Diagrams of bead and tandem insertions with their calculated isodose patterns are shown in Fig. 6. The diagram for the triangular pattern was prepared directly from a roent-genogram of an actual bead insertion. The illustrated "linear" pattern is hypothetical, since none of the actual bead insertions departed that far from the triangular or spherical contour. This hypothetical pattern is included to illustrate the fact that even such a "linear" packing contour has a far lower maximum-to-minimum dosage ratio than does the tandem placement which is also shown in Fig. 6.

NUMBER OF BEADS IN PACK	ROENTGENS PER HOUR AT EXTERIOR WALL OF UTERUS"			
IN PACK	LINEAR PATTERN	TRIANGULAR PATTERN	SPHERICAL PATTERN	
	(0000000000000000000000000000000000000	P @ 00000	P Q	
10	23 35	25 29	28 38	
15 25 35	53 56	40 72	53 75	
50	69 .	88	96	

\*NOTE: THE REFERENCE POINT IS TAKEN TO BE APPROXIMATELY 1,5-cm LATERAL TO THE ENDOMETRIAL SURFACE AT A LEVEL BISECTING THE LENGTH OF THE BEAD PATTERN.

# TABLE I. DOSAGE SCHEDULE FOR CENTRALLY LOADED SPHERES IN A VOLUME PACK -EACH SPHERE LOADED TO AN ACTIVITY OF 15-rhcm-

### 4. Number of Individual Beads in the Volume Pack .--

Any increase in the number of beads in any volume pack of a given contour will significantly alter the dosage schedule. For this reason the number of sources being used, as well as the contour of the pack, must be considered in arriving at an hourly dosage rate at any given point outside the uterine cavity.

For triangular patterns of 25 beads with loading adjusted to give 40 r per hour at a point 1.5 cm. from the endometrial surface, similarly loaded triangular patterns requiring 50 beads will give 88 r per hour at a similar point 1.5 cm, from the inner wall.

There appears to be some advantage clinically in limiting the hourly dose rate to values which will give approximately 1,000 r in any 24 hour period

(i.e., total treatment time of three to four days). Therefore, it is not practical to assume that all patterns and contours can be treated with beads loaded identically, regardless of the number of beads required. In the instance cited, for example, the 25 bead pattern will give about 1,000 r per day, while the 50 bead pattern will give about 2,100 r per day.

# The Dosage Table

In the light of the four factors just discussed, Table I was devised for the estimation of dosages for any given pack pattern for those patterns requiring 25 beads or less. Table II was devised for those patterns requiring more than 25 beads.

Table I assumes individual bead loading of 15 rhcm co<sup>60</sup>. Dose rates are given in roentgens per hour at a point 1.5 cm. from the endometrial surface (point indicated on table headings) for packs of 10, 15, 25, 35, and 50 beads.

Table II is identical with Table I except that the individual bead loading is 7.5 rhem.

The dosage rates are adjusted to give total doses of 2,500 to 4,500 r at 1.5 cm. from the endometrial surface within the time range three to five days, the exact time being determined partially by physical factors and partially by the dosage desired by the clinician.

NUMBER OF BEADS IN PACK	ROENTGENS PER HOUR AT EXTERIOR WALL OF UTERUS*			
IN PACK	LINEAR PATTERN	TRIANGULAR PATTERN	SPHERICAL PATTERN	
	P @ 00000000	P @ 1888	Pa	
10 15 25 35	12 17 26 28 35	13 15 20 36 44	14 19 26 38 48	

\*NOTE: THE REFERENCE POINT IS TAKEN TO BE APPROXIMATELY 1.5-cm LATERAL TO THE ENDOMETRIAL SURFACE AT A LEVEL BISECTING THE LENGTH OF THE BEAD PATTERN.

# TABLE II. DOSAGE SCHEDULE FOR CENTRALLY LOADED SPHERES IN A VOLUME PACK -EACH SPHERE LOADED TO AN ACTIVITY OF 7.5 rhcm-

In actual practice, the purely "spherical" contour as illustrated in Table I leaves much to be desired, inasmuch as the cervical canal and upper vagina would be almost entirely neglected by this placement. The cervical canal should always be filled with beads throughout its entire length.

### Use of the Dosage Table

After the uterine packing is carried out as described earlier, pelvic anteroposterior and lateral roentgenograms are made. From these films it is determined whether the contour approximates the linear, triangular, or spherical form. Knowing the number of beads in the pack and the form of the pack, the dosage in roentgens per hour may be found from the table. The total treatment time may then be calculated easily by dividing the desired total dose by the dose rate.

TREATMENT TIME (hours) =  $\frac{\text{DESIRED TOTAL DOSE (roentgens)}}{\text{DOSE RATE FROM TABLE (roentgens per hour)}}$ 

# Clinical Discussion and Summary

A method has been devised for the uniform application of radiation to the uterus in endometrial carcinoma. Multiple sources encased in stainless steel spheres are used to pack the uterine cavity. Uniformity in filling of the uterine cavity tends to avoid the danger of overtreatment of nonuterine tissue at any point. The dosage table provides a simple means of estimating the time required to deliver any desired dosage.

We would like to express sincere thanks to Mr. J. Y. Smith for his many helpful suggestions.

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### Discussion

DR. WILLIS E. BROWN, Little Rock, Ark .- The authors have presented a fine review of preoperative irradiation in endometrial carcinoma and a novel approach to its solution. The traditional concept of so many minutes of x-ray therapy, or so many milligram hours, is being replaced by more precise measurements. This is true for both external irradiation by x-ray and internal irradiation by gamma roentgens. It is no longer adequate to talk in terms of roentgens in the air or milligram hours; one must consider the filtration, time of administration, the distance of penetration, back scatter, and other similar features in attempting to appraise correctly both the plan for and effect of irradiation.

I wish to discuss two factors: (1) the principles and the theory of preoperative radiation in endometrial carcinoma, and (2) the various technical aspects of this type of therapy.

The results in those clinics employing preoperative irradiation are approximately equal to those using surgery alone, and show only a slight advantage over the use of external and internal irradiation alone. Second, there is extremely poor correlation between the dosage of intrauterine irradiation and the results obtained. In fact there is some evidence to show that there is perhaps a reverse correlation and the concept of a supralethal theory has again been introduced. Third, we find very poor correlation between tumor survival in the excised specimen and the over-all survival of the patient.

Perhaps the function of preoperative irradiation is not cancerocidal, but designed to improve the local hygiene. Certainly intrauterine irradiation does temporarily remove fungating masses of carcinoma which are usually secondarily infected. Likewise it shrinks the local tumor, facilitates surgery, and, perhaps to some extent, will limit the spread of the tumor during this interval of local improvement.

We use preoperative irradiation at the University of Arkansas School of Medicine in the treatment of endometrial carcinoma, but believe that its effect is primarily a local hygienic one rather than of cancerocidal benefit. Perhaps the use of preoperative irradiation as a cancerocidal agent still needs verification.

When attention is turned to the technique of preoperative radiation, there are a number of factors which must be considered. Not only is the dosage important, but the distribution throughout the uterus and tumor mass as well as the protection of other viscera must be considered. The technique presented by Hendricks is unique and



Fig. 1.



Fig. 2.

Figs. 1 and 2.—These are anteroposterior and lateral roentgenograms of the pelvis with gamma foci in place. The round shadow just above the symphysis on the anteroposterior film is sodium iodide in the balloon of a Foley catheter. The skin clip represents the margin of the cervix. The confused overlapping shadows in the midpelvis on the anteroposterior film are formed by the superimposed shadow of barium in the rectum and foci in the uterus. In Fig 2, sodium iodide in the Foley catheter is visible on the film, but did not show up in the reproduction.

From these two projections calculations as to distribution of radiation throughout the uterus and fetus can be made.

facilitates the proper distribution of gamma radiation throughout the uterine cavity. There is some question in my mind, however, that in a very large uterus the large number of beads might provide an excessive total radiation that would be somewhat hazardous, and raises the possible advantages of external irradiation as a preoperative preparation.

Our technique is quite similar to that of the authors in that we employ multiple small foci. It is apparent that the distribution of the foci cannot be as effective as the bead technique. There is one feature which I believe warrants our consideration, namely, the calculation of radiation in the total volume of the uterus, and the protection of the surrounding bowel and bladder from excessive irradiation. This is done by the use of anteroposterior and lateral roentgenograms taken after the insertion of the foci, utilizing contrast media within the bladder and rectum. (Figs. 1 and 2.) By this method we can with some accuracy calculate the gamma roentgens delivered throughout the uterus and surrrounding viscera and be able to determine with some accuracy the minimum and maximum radiation delivered. Hendricks' utilization of the multiple bead foci obviously provides better distribution. Perhaps some protection can be provided by the use of similar film studies.

In contemplating the matter of distribution, I wonder whether or not the use of external irradiation with the higher-voltage machines and the recently available Telecobalt bombs may not produce the best distribution throughout the pelvis and uterus. It is of interest in this regard that some clinics still employ external irradiation as the preoperative preparation of choice, and the results apparently are approximately the same as with the other techniques.

Failures in the cure of endometrial carcinoma are usually the result of unsuspected clinical extensions. There may be unsuspected extrauterine spread to the tubes, ovaries, and pelvic peritoneum which cannot be detected by preoperative clinical examination. Obviously intracavitary forms of therapy are of no value in this type of patient. It is doubtful if external irradiation could deliver a sufficient cancerocidal dose to be of much help under these circumstances, although it is more likely to be beneficial than the more limited form of intracavitary treatment. It appears that in patients with large uteri, a long history of bleeding, and a high probability of extrauterine extension, external irradiation alone or in combination with intracavitary irradiation may prove a more satisfactory preoperative preparation.

The second source of failure is recurrence or residual carcinoma within the paracervical triangle and the vaginal cuff. We believe that some form of irradiation therapy is needed in this area. There are obviously many methods of accomplishing this; the use of a plaque, the vaginal colpostat, or, as employed in our clinic, a capsule of radium placed within the cervical canal flush with the external os has proved fairly satisfactory. We believe that this is an important adjunct in the radiation therapy of endometrial carcinoma since it is the most common area of local recurrences.

DR. A. N. ARNESON, St. Louis, Mo.—Novak has appropriately stated that the treatment of endometrial cancer is a rather fluid problem. I think we might say with equal appropriateness that some stability is being reached.

To be sure, the instability of the question of treatment falls chiefly in the group of patients who are acceptable for surgery; that is, whether or not they should first be given preoperative radiation.

To a limited degree, the fluid problem also falls in the method of radium treatment for patients to be treated also with surgery, or to be treated by radiation alone.

Sherman and I have just finished a review of the endometrial cases over the past several years, and we came—with validity—to the conclusion that preoperative radiation helped materially in certain cases. To be sure, in a patient with the early lesion, presenting a small uterus with an undifferentiated type of tumor, it is not possible to demonstrate any improvement with preoperative radiation, but among those with the large uteri, or among those with undifferentiated tumors, we thought we had conclusive evidence that preoperative radiation did contribute to an improvement in results.

Now, without going further—as Brown has done—into the factors that might lead to betterment in the prognosis of preoperative radiation, I think it is well to turn here to the particular technique or method of radium treatment Hendricks has described, which seems to me to be a definite advance.

If radium is to be applied in the small uterus, probably the tandem method is a fairly satisfactory one. Certainly, in the small uterus, for the insertion of multiple capsules of some size, the technique is difficult. The number of tubes that can be put in is always few. Hendricks has a means of increasing the number of sources to be gotten into the small uterus.

If I am quoting correctly the impression of some physicists, they have labored under certain impressions. If you will go back just for a moment to Heyman's technique, he utilizes a scurce of over-all size with small dimensions. Inside that source there is a central area containing a tube of radium. Around that tube of radium there is a delicate framework supporting an outer shell. The aim of that is to provide some distance between the radium and the outer surface of the applicator.

Brown's tubes are cumbersome, and it is difficult to get very many tubes into the uterus.

Would shortening the length of the tubes of radium improve the distribution, exactly as Dr. Hendricks' method does?

When one gets into distances of 1 or 1.5 cm. away from the inner lining of the uterus, that is not very important.

I wish to ask Dr. Hendricks if he is of the opinion that the distribution of radiation, let us say, on the surface of the uterus—which may or may not be important, clinically—differs materially from that which he might expect from a coarser type of applicator.

I also wish to ask him if he has had any difficulty in removing these strings. I should think they would be extremely easy to remove, which is not true for the ordinary type of capsules, with which there may be difficulty.

Finally, I wish to ask if he utilizes any radiation in the vagina. We felt it was rather important to supplement the dose given there.

DR. HENDRICKS (Closing).—Dr. Brown said it almost seems as though the smaller the dose of radiation, the better the results. That is almost what we are trying to say in this paper, so we tend pretty well to agree with him.

Our only point of disagreement with Dr. Brown is that we still feel that some form of radiation—perhaps his preoperative preparation—is a very valid thing, and as far as we can see, it is a fairly necessary part of the most effective available management of endometrial carcinoma.

We agree with Dr. Arneson when he says that the tandem in the small uterus is a fairly satisfactory form of therapy. That is true because in using a small tandem in a small uterus, where the entire length of the uterus is filled by the tandem, the largest maximum-to-minimum dosage is approximately 4 to 1. That is not too bad if we assume we do not have to kill every single tumor cell prior to the time of hysterectomy. Of course, where the tandem becomes woefully inadequate is in the use of a single tandem in a large uterus, where the maximum-to-minimum dosage can go to as high as 10 to 1 at various places on the uterine surface. Under those circumstances, certainly, either there is going to be severe overtreatment of some nonuterine tissue, or else some areas are going to be entirely neglected, for practical purposes.

As to whether or not the distribution of radiation on the surface is improved in this type of applicator, I do not think there is a good answer to that, except to say that we believe the distribution is improved to the degree that the multiple sources form a homogeneous body of material. It is almost like the equivalent of a fluid mass. It can be entirely uniform in that way.

There has been no difficulty in removing any of these bead insertions. Occasionally there is difficulty in inserting the beads, and we found that to be almost entirely due to failure to get adequate dilatation up to the level of the interior os. Once that is obtained, the actual insertion of the beads is a reasonably easy procedure.

We, too, believe that this treatment or any other treatment should include some form of radiation of the upper vaginal area prior to total hysterectomy.

### PHEOCHROMOCYTOMA COMPLICATED BY PREGNANCY\*

J. WILLIAM PEELEN, M.D., F.A.C.S., AND A. DE GROAT, M.D., KALAMAZOO, MICH.

(From Borgess Hospital)

THE presence of pheochromocytoma in association with pregnancy has been noted only twenty-nine times in the literature. The primary purpose in discussing this subject is to stress the seriousness of its effects on the fetus and the mother.

Briefly, pheochromocytoma is a lesion affecting the chromaffin tissue in the body located in the adrenal medulla and along the course of the great vessels in the abdomen and chest. In nine out of ten patients it involves the medulla of the adrenal and more commonly on the right than the left. The tumor may be silent without any symptoms, but more frequently it secretes varying amounts of pressor substances which produce a paroxysmal type of hypertension or persistent hypertension or both.

The diagnosis of pheochromocytoma was made only at autopsy for thirty years after the condition was first described by Frankel<sup>1</sup> in 1886. Pincoffs<sup>2</sup> was the first to report a case in 1929 in which the preoperative diagnosis was pheochromocytoma and the patient was operated upon successfully. Since then over three hundred cases have been reported in the literature. Smithwick<sup>3</sup> reported the incidence of pheochromocytoma in a group of hypertensive patients to be about 0.5 per cent. Accordingly he estimates that we can expect from six hundred to eight hundred patients with pheochromocytoma every year. The disease affects both sexes almost equally and is more frequent between the ages of 20 and 40 years. This being the main childbearing period, we should expect to see it during pregnancy.

Clinically, it is usually characterized by sudden attacks of headache, anxiety, nervousness, palpitation, substernal pressure or pain, followed by exhaustion and profuse sweating. Nausea, vomiting, and abdominal and leg cramps occur at times. The attacks may last from a few minutes to several days. It is not uncommon for the attacks to occur at night or when the patient is under great stress. The attacks occurring in one individual follow a fairly definite pattern for that patient, although they may vary in intensity.

After a preliminary diagnosis is made there are tests that are used to confirm the diagnosis of pheochromocytoma. Some drugs can bring on the attacks and are known as provocatives and others are known as antagonists and are antagonistic to the pressor amines. Recently Goldenberg,<sup>4</sup> reported another aid in the diagnosis by determining the catecholamines in the urine.

<sup>\*</sup>Presented at the Twenty-second Annual Meeting of the Central Association of Obstetricians and Gynecologists, St. Louis, Mo., Oct. 7 to 9, 1954.

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He reports "no false negative or false positive tests using the method of adsorption on precipitated aluminum hydroxide plus photo-fluorometric evaluation."

The problem of locating the tumor follows the confirmation of the diagnosis. Nine out of ten tumors are in the adrenals. The more common diagnostic aids are a plain roentgenogram of the abdomen and an intravenous pyelogram. Only a small percentage have been located by palpation. The average size of the tumor is that of a lemon. The size of the mass is no indicator of the severity of the condition. For more detailed study of pheochromocytomas we refer you to papers by Graham,<sup>5</sup> Cahill,<sup>6</sup> Kvale, Priestly, and Roth.<sup>7</sup>

The variable clinical manifestations of the disease makes it difficult to diagnose; therefore, one has to be suspicious of this clinical entity. The reason for the variation in symptoms has been ably demonstrated by Goldenberg<sup>8</sup> in his experimental work on human beings by injecting epinephrine and norepinephrine in varying amounts and thereby obtaining variable symptoms.

During pregnancy pheochromocytomas frequently produce symptoms similar to toxemia of pregnancy and after delivery those of shock, cerebral damage, uterine rupture, or postpartum hemorrhage. A total of twenty-nine pregnancies occurring in nineteen patients have been reported. Signs of toxemia of pregnancy were usually the first evidence of trouble. Before reviewing the literature the following case, which occurred in our practice, is presented.

Mrs. V., aged 27 years, gravida ii, para i, was first seen on Oct. 26, 1953. Her last menstrual period began on Aug. 10, 1953. The patient's only previous pregnancy terminated normally nine years before. According to her story the past personal history was negative. After the patient died, however, we obtained the following history from the husband. Her first attack occurred in 1948. She was under extreme mental strain. The headache was so severe it stunned her. She went to a doctor for a few months and he gave her nerve tablets. The attacks of headaches kept recurring frequently until October, 1949. She was under severe mental strain-all this time. Then she located in another city and seemed much happier and the attacks were much less frequent. During the summer of 1952, after a few marital difficulties, the headaches were more frequent. In January, 1953, the patient was in an automobile accident. She did not sustain an injury but was in shock, according to the husband. The attacks were more frequent for a few months.

After she became pregnant the attacks increased. Headaches would occur almost after every meal. She would vomit and then feel all right. In addition she had other attacks occurring at night, which he described as follows: When the headache occurred she would stiffen and roll on her side. She did not have as many attacks when she slept on her left side, but when she lay on her right side or on her back she was likely to have more attacks. During the headaches her face would turn very pale, her heart would pound. After the headache stopped, her color would return, she would shake all over and feel very weak and warm, and perspire lightly. During pregnancy she was attended by a chiropractor for the headaches. She did not mention this to us because all the physicians she had seen before had told her they were due to nerves.

Her prenatal course was uneventful until three days before admission. Her total weight gain had been 12 pounds and the blood pressure was normal throughout until the day of admission in the thirty-fifth week. Three days before she said it felt like she had something in her right eye that she could not get out. The next two days her vision became progressively worse. The following morning her face was flushed and she could hardly see when she came to the office. The blood pressure was 158/100 and the urine contained 2 plus albumin.

Upon admission to the hospital one hour later the blood pressure was 200/130. The patient did not complain of any more headaches after the blurring began. She was seen by Dr. Max Finton who reported a 4 plus papilledema and retinal hemorrhages. He recommended that pregnancy be terminated before more damage occurred to her eyes. After another hour the blood pressure was 230/150. It was decided to terminate pregnancy. The cervix was hard and not effaced and she was prepared for section. It was noted that the patient appeared very flushed when she was brought to the operating room, but no significance was attached to this at the time. Spinal anesthesia was given. Just before the operation was started the blood pressure had gone to 260/150. A low cervical cesarean section was done without any difficulty and a normal male infant was delivered. The patient was returned to her room in good condition with the blood pressure 195/150.

Thinking we were dealing with a rapidly progressive toxemia of pregnancy, we narcotized her fairly heavily. Seven hours after surgery, the pulse pressure was twenty with blood pressure 140/120. At 5:00 a.m. the blood pressure was the same and all extremities were cold, and the body very warm. The temperature was 104.5° F. and the pulse rate 160 per minute. She was alert and stated she felt fine. At 6:00 a.m. the temperature was 106.8° F. orally. We were unable to obtain the blood pressure at 9:00 a.m. and the patient was unconscious. An electrocardiogram taken by Dr. E. Betz revealed evidence of auricular fibrillation. She was digitalized quickly. This slowed the heart rate temporarily. The rectal temperature was 109° F. at 11:00 a.m. She remained in this condition until shortly before she died, when consciousness returned and she was able to talk.



Fig. 1.—Pheochromocytoma. Gross specimen.

Our differential diagnosis in the last 24 hours included cerebral hemorrhage, brain tumor, and cardiac failure. We did not think it was eclampsia after the temperature became elevated, in addition to the complete peripheral circulatory collapse.

The positive findings at autopsy by Dr. Hazel Prentice were as follows:

Gross .-

Lungs: The lungs were moderately bulky and normal except for extreme passive congestion in the posterior parts of the lobes and frothy fluid in the trachea and bronchi.

Adrenals: The left adrenal gland measured about 3.5 by 2.5 by 3 cm. The right adrenal was stretched low with the surface of a tense spherical cyst, about 6 cm. in diameter. When the cyst was opened, blood spurted out under some pressure from a central area. There was a wall of red and gray tissue which was extremely hemorrhagic and which reached a thickness of about 1 to 2 cm. It had the appearance of central hemorrhage in a previously solid tumor.

Microscopic.

Lungs: Congestion was intense and general and most of the alveoli contained some albuminous material. In addition to this, there were patches where the alveoli were filled with polymorphonuclear leukocytes,

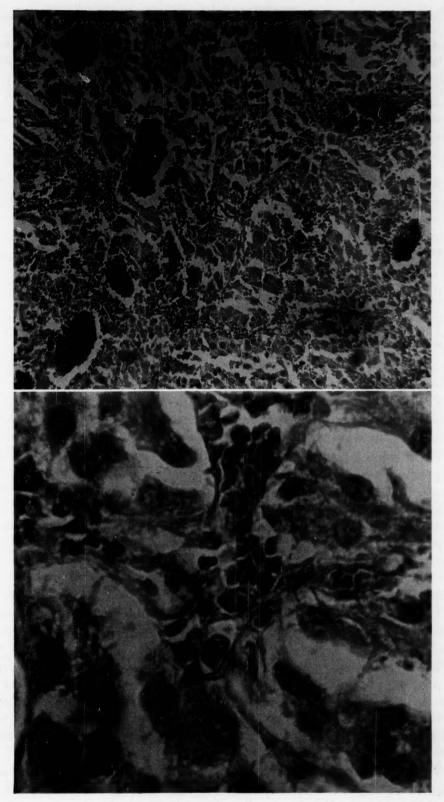


Fig. 3.

Fig. 2.—Note vascularity of tumor. ( $\times 254$ ; reduced  $\frac{1}{6}$ .)
Fig. 3.—Polyhedral cells with large nucleus and abundant cytoplasm. ( $\times 1310$ ; reduced  $\frac{1}{6}$ .)

Adrenals: The tumor of the adrenal was composed of large polyhedral cells with abundant pale pink granular cytoplasm, much larger than the cells of the normal adrenal cortex. They varied somewhat in size, were not particularly hyperchromatic and were vesicular; no mitotic figures were seen. The vascularity was great and the blood spaces were of capillary type and dilated. There were also some interstitial hemorrhages.

Pathologic Diagnosis.—Pheochromocytoma of right adrenal gland; pulmonary edema, and bronchopneumonia.

### Comment

Reports<sup>9-26</sup> on 19 patients with simultaneous pheochromocytoma and pregnancy were found in the literature. These 19 patients had a total of 29 pregnancies while the tumor was present. During the remainder of this report, we will include our case.

The maternal mortality was 9, or 45 per cent. One mother died undelivered and the other 8 died within seventy-two hours after delivery. In addition, one patient died one month later following operation and another died eighteen months later while waiting for surgery.

The symptoms most suggestive of pheochromocytoma were paroxysmal in 16 of the 20 patients. One had persistent hypertension. The type of symptoms was not noted in the other 3 cases. The youngest patient was 20 years of age and the oldest was 35.

The diagnosis of pheochromocytoma was confirmed in each of the 20 patients either at surgery or autopsy. The tumor was located in the right adrenal in 9 patients; in the left in 9; and 2 patients had bilateral tumors.

The incidence in the three trimesters of pregnancy was as follows: first, one patient; second, 4 patients; third, 25 patients. We have included the pregnancies that terminated during the first two trimesters because symptoms of pheochromocytoma complicated by pregnancy may occur that early. One patient died when only four months pregnant; another of the same duration of pregnancy had no attacks while she was pregnant but they were much more severe afterward than they had been before the pregnancy started; and a third patient had labor induced at six months because her complication was diagnosed as chronic nephritis. She was delivered of a macerated fetus.

Twenty-five pregnancies terminated in the last trimester. Seventeen babies, or 68 per cent, were born alive. There were 8 stillborn infants, which included one with a fetal abnormality.

The diagnosis of toxemia of pregnancy was made in 15, or 50 per cent, of the pregnancies; eclampsia in 2; chronic nephritis in 2; nervousness and hysteria in 5; and no diagnosis mentioned in 6. Disturbances in vision occurred during 10 of the pregnancies. This was the most prominent finding during several of the pregnancies. It was not mentioned in the other 20 pregnancies.

There is some evidence that hypertrophy of the adrenal cortex occurs during pregnancy but this has not been found to occur in the medullary portion of the adrenal. It is known that, during pregnancy, enlargement of some tumors may occur. Is it possible that the abnormal chromaffin tissue present may be stimulated to produce these unusual symptoms? If this should be the case, it could not account for the absence of all attacks in several patients while they were pregnant.

Before delivery the findings were very similar to those of toxemia of pregnancy. The patients may have convulsions like those we see in eclampsia. Also, profound shock may occur. This must be differentiated from shock which occurs with rupture of the uterus and postpartum hemorrhage.

The occurrence of pheochromocytoma and pregnancy simultaneously is more than a coincidence. The cases reported are far too few for evaluation.

### Summary

- 1. A case of pheochromocytoma complicated by pregnancy, with a fatal outcome for the mother, has been reported.
- 2. A total of nineteen patients with pheochromocytoma who had twentynine pregnancies while the tumor was known to be present are reviewed.
- 3. The symptoms of toxemia of pregnancy and those found in pheochromocytoma complicated by pregnancy are discussed.
- 4. The symptoms of postpartum hemorrhage, rupture of the uterus, and those which occur after delivery in patients who have pheochromocytoma are very similar.

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### Discussion

DR. J. C. CARMICHAEL, Birmingham, Ala.—The essayist has directed our attention to a medical problem which may present a grave hazard to the obstetric patient. At our Medical College of Alabama there has been no diagnosis of pheochromocytoma in 21,205 obstetric patients, in spite of the fact that significant hypertension has been observed in 2,301 patients. If we accept Smithwick's estimate that pheochromocytoma is responsible for one out of every two hundred cases of hypertension, then we have overlooked perhaps eleven cases of hypertension due to this tumor.

We have had deaths from hypertension, many without autopsy. It is quite likely that in some of our most serious problems we have failed to recognize the basic pathology.

Diagnostic procedures are available everywhere. Their utilization in suspicious cases should turn up many of these tumors every year.

DR. McCRARY.—Pheochromocytoma complicating pregnancy is still uncommon. Its recognition often is in retrospect and exposes the patient to a high maternal and fetal loss as noted by Dr. Peelen. The early diagnosis of this tumor, before more pregnancies are encountered, would improve our statistics, since this condition can be cured by surgery.

I have recently submitted as coauthor a follow-up report of a case of pheochromocytoma and pregnancy previously noted in the literature. This report will appear in a future edition of The Journal of the American Medical Association. I wish to add some of our findings in this case to today's discussion. Our patient had three pregnancies which went to term but she developed hypertension, alubminuria, and edema in the last trimester of each. She returned to normal after the first and second pregnancies, but following the third gestation her hypertension persisted. The diagnosis had been made with each of these pregnancies of toxemia of pregnancy, but because of the persistent hypertension she was studied further and the diagnosis of chronic glomerulonephritis was made. As a result of this diagnosis her fourth pregnancy was interrupted. The correct diagnosis of pheochromocytoma was not made until five years following the initial onset of symptoms. The true nature of the disease was finally suspected because of her complaints of frequent and severe headaches, excessive perspiration, and nervousness. The patient had surgical exploration with removal of a unilateral pheochromocytoma involving the left adrenal. Following this she became clinically and symptomatically well. She has subsequently had two pregnancies, the first one a spontaneous abortion at three months, and the second a full-term normal pregnancy, fifteen months following surgery. At no time during this last pregnancy did she develop hypertension, albuminuria, or edema. She is well at present.

The symptoms and signs of pheochromocytoma occurring in the third trimester, and their resemblence to the signs and symptoms of pre-eclampsia make it easy to understand the erroneous diagnosis of pre-eclampsia in the fifteen cases noted by Dr. Peelen. This error of diagnosis might seem to justify a routine benzodioxane, Regitine, or histamine test in the diagnostic workup of a suspected case of toxemia, especially if there is hypertension plus glycosuria, hyperglycemia, and/or excessive perspiration.

There are multiple reports of surgical cures of pheochromocytoma. To my knowledge, our patient is the second to have a successful term pregnancy following surgical removal of the tumor. This was maintained with no special medications, and shows that "surgical cures" remain "cures" under the stress of pregnancy.

The paroxysmal attacks of pheochromocytoma are reported to occur frequently as a result of anoxia. I have been taught that conduction anesthesia is contraindicated in patients who have an unstable vascular system, because of the sudden profound hypotension or shock state that may result from the block. I wish to ask Dr. Peelen if this situation developed as an anesthetic problem in his case.

The presence of a pheochromocytoma, whether it be malignant or benign, may at any time cause unexpected death. Once this diagnosis is made, the best treatment seems to be

surgical removal of the tumor. We do not have many cases to learn from, and I would like to know what your recommendations would be, Dr. Peelen, in a case with intermittent hypertension and, second, in a case with persistent hypertension, that is positively diagnosed as pheochromocytoma in the first or second trimester of pregnancy?

DR. TOBY LEVITT, London, England.—In a study of over 4,000 consecutive thyroidectomies, I was very intrigued by the coexistence of thyrotoxicosis with pheochromocytoma, with the known simulation of thyrotoxicosis by the toxemia of pregnancy.

I was interested by the fact that two of these cases were diagnosed as thyrotoxicosis when, in fact, they were pheochromocytoma, the chief reason being that it is so easy to see the thyroid and so difficult to see the adrenal.

Therefore, may I make a plea that, in these cases where thyrotoxicosis is diagnosed under such circumstances, further investigations be made to elucidate a probably deeper cause of this condition.

DR. PEELEN (Closing).—I am glad that Dr. McCrary asked the question about what we would do with this condition if we found it during pregnancy. If the anesthetist had been alert, we would have detected an abnormality when we started our cesarean section—when the blood pressure went up.

The patient with pheochromocytoma may be entirely asymptomatic prior to a fatal attack.

I think that, if we find a pheochromocytoma during pregnancy, we should treat it and ignore the pregnancy.

# ADRENOGENITAL VIRILISM WITH ADRENAL CORTICAL HYPOFUNCTION\*

# A Clinical Entity

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DEVIATIONS in sexual differentiation are rare in spite of the complexity of the process involved. When they do occur, however, they may present an almost inscrutable enigma to the physician, as well as a tragic and difficult situation for both parents and child. Abnormalities of this nature, when coupled with serious illness in the child, present to the physician the almost overwhelming temptation to do nothing, hoping that death may resolve the dilemma.

It is our belief that the combination af adrenal virilism with adrenal cortical hypofunction is a definitely recognizable syndrome, and that modern knowledge of the adrenals offers at least a chance for life and for normal development. The review here presented, together with a report of three cases encountered in private practice, is compiled in the hope that it will call the attention of all obstetricians to the syndrome.

### Case Reports

CASE 1.-N. J. H. was a full-term infant born Nov. 7, 1947. The course of the mother had been completely without incident. Two previous pregnancies had resulted in normal full-term male infants. Labor was short, of one hour and fifty-one minutes' duration. The baby weighed 3,487 grams, breathed spontaneously, and was apparently completely normal except for an abnormality of the genitals. This consisted of a penislike structure approximately 3 cm. in length. On either side there were large scrotumlike labial folds. At the base of the clitoris there was a small opening on the anterior wall of which could be seen a small orifice. No testes were palpated. With some hesitation the sex was declared as female. The baby apparently did well in the hospital, although weight gain was slow, and was released with the mother on the seventh day. On the tenth day, however, there was noted the onset of lethargy, and the baby took fluids and formula poorly. On the thirteenth day the infant took only 5 ounces of formula in a twenty-four-hour period. She was returned to the hospital where she was given parenteral fluids in an effort to maintain fluid balance. She did not do well, however, and on November 29 was transferred to another hospital. Here the examination showed an emaciated, dehydrated infant who weighed 2,807 grams. The liver was palpable three finger breadths below the costal margin, the spleen was palpable, and the genitals were as previously described.

Hematological studies were normal. The nonprotein nitrogen was 47.5 mg. per cent, serum chlorides 67 meq., potassium 9.5 meq., sodium 144 meq. X-ray of the chest showed bronchitis. A flat plate of the abdomen was negative. There was no evidence of bone abnormality. The electrocardiogram showed changes consistent with potassium intoxication. The 17-ketosteroids were 2.357 mg. (normal 0 to 0.5). In spite of fluids up to 1,700 c.c. daily, dehydration kept recurring. Once established, a total of 1,000 c.c. of fluids

<sup>\*</sup>Presented at the Twenty-second Annual Meeting of the Central Association of Obstetricians and Gynecologists, St. Louis, Mo., Oct. 7 to 9, 1954,

was given daily with 3 to 5 Gm. of sodium chloride and this maintained fluid balance. On the sixth hospital day the patient became cyanotic, developed a few coarse râles, and died within a matter of minutes.

Autopsy.—The body was that of a poorly nourished infant with the external genital changes previously described. On opening the body, a bicornuate uterus and normal tubes and ovaries were found. The adrenal glands were grossly enlarged, weighing 20 grams (normal 10). The cortex appeared gray and granular, and the normal architecture was distorted.

Histologically the adrenals showed the only change. The cortical elements were unusually prominent and zonal distribution was not distinct. The inner or androgenic zone was prominent and showed many large, pale, red-staining cells. The medullary cells were scanty. Section through the pituitary gland showed marked prominence of the basophilic cells.



Fig. 1.—(Case 3) Detail of genital anomaly common to all three cases.

Case 2.—G. L. D. was the second child of a normal 24-year-old mother, born Nov. 2, 1949. The first baby was normal and a subsequent sibling is also normal. The present pregnancy was completely without incident, terminating at term in a normal labor of two hours and thirty minutes. The infant weighed 3,487 grams and appeared completely normal, except for an abnormality of the genitals. The clitoris was abnormally large, with large scrotumlike labial folds. At the base of the clitoris there was a canal, in the anterior wall of which could be seen a small opening. The course in the hospital was normal, except that the nursing notes indicate that the baby was lethargic and sleepy, was chronically constipated and dehydrated, and failed to gain weight. At home the baby continued to present a feeding problem and to be sleepy and lethargic. At the age of 2 months, she was admitted to the hospital. Examination at this time confirmed the genital changes described above, and was otherwise negative except for the generally poor nutrition and hydration observed.

The blood count and urinalysis were normal. The nonprotein nitrogen was 30 mg. per cent. The blood sugar was 69 and on a later date 92 mg. per cent. The carbon dioxide combining power was 26.4 volumes per cent and later 30 volumes per cent; serum sodium 126 meq., potassium 6.4 meq., 17-ketosteroids 9.025 mg. The electrocardiogram and pyelograms were normal.

The infant was treated with parenteral fluids, but was released from the hospital on January 24 (the sixth hospital day) before further contemplated studies were obtained.

On Feb. 5, 1950, the child was readmitted. She had continued to do poorly at home and had been lethargic and sleepy. Laboratory studies at this time showed the blood count and urinalysis to be within normal limits. The nonprotein nitrogen was 42 mg.

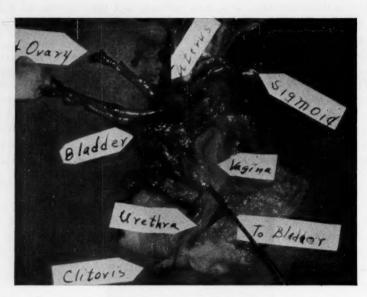


Fig. 2.—(Case 3) Common urethra and vagina, with normal female genitals.

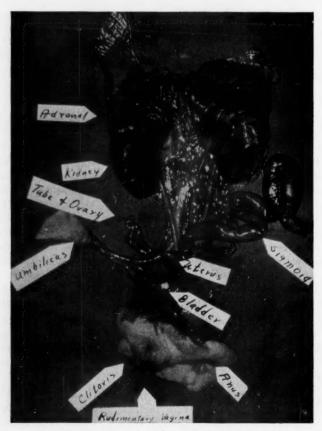


Fig. 3.—Hyperplastic adrenals from Case 3. Note that they appear as large as do the kidneys.

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per cent, sugar 145 per cent, sodium chloride 415 mg. per cent, urea 23 mg. per cent, and uric acid 3.7 mg. per cent. The glucose tolerance test was normal. Serum sodium was 127 meq., potassium 7.2 meq. The Thorn test indicated failure of the adrenals to respond to epinephrine. On December 23 the patient developed epidemic diarrhea and vomiting without fever. Her condition deteriorated progressively, and death ensued on Dec. 25, 1950.

Autopsy.—(Positive findings only.) The body was that of a poorly developed and nourished infant of 13½ months. There was profuse hairy development of the body. The genitals were as described previously. Normal female organs were present. The only abnormality in the viscera was the adrenal glands which were unusually large and weighed 10 grams each. Histologically the cortical tissues were hypertrophic with a scanty medulla. Nests of cortical cells were found in the capsule.

CASE 3.—P. was the first child of a normal white woman. The pregnancy was uneventful. Two weeks prior to the expected date of confinement spontaneous labor ensued, and after an eighteen-hour labor, delivery of a 2,268 gram infant was effected by outlet forceps. The baby appeared completely normal except for a genital anomaly. This consisted of an enlarged penislike structure which measured 1.5 cm. in length. On either side there were large scrotumlike labial folds in which there could be palpated no masses. At the base of the penislike structure there was an opening on the anterior wall of which could be seen a small orifice.

The baby was placed on a routine for prematures consisting of oxygen in incubator, Hykinone, and penicillin. In spite of this the weight declined steadily. Two days after birth the infant was started on 50 c.c. of normal saline subcutaneously and this was continued to the end. The baby was listless, took fluids poorly, and was chronically dehydrated. The weight declined in spite of formula changes. There were episodes of diarrhea. Laboratory work was confined to blood studies which were normal, and a blood culture which was reported as positive for growth of alpha streptococcus. On October 23 the patient was started on desoxycorticosterone acetate, 2 mg. daily. On the following day, however, the temperature went to 100° F. and on October 25 to 101°, and the infant died on Oct. 25, 1953, at 1 month of age (Figs. 1 to 3).

Autopsy.—Grossly the anomaly previously described was noted, in addition to a normal uterus, tubes, and ovaries. There was no evidence of testicular tissue. The adrenals were grossly enlarged, the left weighing 7.5 grams and the right 6 grams. Microscopically there was a marked preponderance of cortical elements with a well-defined zona reticularis, and a questionable area of condensation of this zone in the inner portion nearest the almost absent medulla.

### Comment

Incidence.—The incidence of this particular anomaly is low. In 1949 Zuelzer and Blum¹ found 17 cases reported in the literature. Since then 11 additional cases have been reported,¹-5,¹8 which with the 3 here reported, bring the total to 31 cases. Zuelzer and Blum believe, however, that the actual incidence is much higher than these figures indicate. In their own material they estimate it as varying from 0.37 to 0.52 per cent. In our own practice this syndrome has been encountered three times in 5,454 deliveries, an incidence of 0.055 per cent.

Etiology.—The problems of intersex in general, and of this syndrome in particular, have offered free grounds for wide speculation. Normal sexual patterns are probably determined by purely genetic factors, and, conceivably, variations in these factors could cause an infinite variety of aberrations. In cases of intersexuality where no hormonal factors can be demonstrated, genetic

factors are probably at fault. It has been demonstrated, however, 6, 9 that contrahormone therapy in both male and female rats can produce retention of the sexual elements of the other sex. In the female adrenal pseudohermaphrodite, the genital tract undergoes modification of its caudal end which closely resembles that which can be induced in animals by hormone treatment. These patients do not, as a rule, however, show persistence of male elements, and hence the hormonal modification must come into effect shortly after the differentiation of the duct system. In the adrenal female intersex with hypocortical function this hormonal factor is thought to be from the hyperplastic adrenal.

The adrenal cortex elaborates some 42 hormones which can be roughly grouped in three functional units: (1) anabolic-androgenic, represented by the 17-ketosteroids; (2) catabolic-gluconeogenetic hormones, represented by the 11-17 corticoids; and (3) electrolytic, electrolyte and water maintenance.

Many men believe that these functions may be contained in recognizable histological portions of the gland. Thus, the zona glomerulosa cells regulate the electrolytes, the zona fasciculata the carbohydrate mechanism, and the zona reticularis the androgenic functions. In addition, in the fetal adrenal, an androgenic zone has been described lying between the reticularis and the medulla, which is thought to be the fetal sex organ, and has been described as persisting in neonatal life in those patients who have a disturbance in androgenic function. Zuelzer and Blum speculate that the portions of the gland responsible for carbohydrate mechanisms are unchanged, and that the cells of the glomerulosa, which normally regulate electrolyte balance, are replaced by the pale eosinophilic cells of Broster and Vines which are the androgenic cells. This, of course, would account on a histological basis for all the clinical signs. Unfortunately histological evidence as to the presence or absence of the zonal alterations is by no means uniform.

Familial Tendency.—A number of authors have pointed out a fact that is important to the obstetrician, namely, that there is a strong tendency toward familial recurrence. Biggs and Rose<sup>10</sup> found 9 families recorded in each of which two sisters were pseudohermaphrodites, and 4 additional families in which both male and female siblings were affected. Hinman,<sup>11</sup> in his review of the problem, found that of 154 intersexes of various types, there were 51 in whom there was clear evidence of familial tendency. Of the 4 cases reported by Zuelzer and Blum there was a family history in 2. In the cases here presented no such definite trend could be seen; in two cases, however, all other siblings were male, and in the other case the patient was the only child.

Clinical Signs and Diagnosis.—The finding of a feeding problem in an infant with a genital anomaly of the type described is almost pathognomonic of the diagnosis. The infant in the early days of life demonstrates lethargy, failure to take food well, dehydration, and occasionally diarrhea and constipation. Progressive weight loss is noted.

Since there is an accentuated action of the androgenic portions of the gland, and a malfunction of the electrolyte-maintaining portion, laboratory tests will show an increase in the daily output of 17-ketosteroids. If fractional determina-

tions are done the alpha factor will predominate. The 11-17 corticoids are unchanged. Serum sodium and chloride levels are low and serum potassium is elevated. The blood nonprotein nitrogen as a rule is high and the blood sugar and glucose tolerance tests are within normal limits.

Numerous methods have been suggested for determining the true sex. Cystoscopic examination and uterotubography have been used.<sup>12</sup> Adrenal aerograms may reveal the gross adrenal hyperplasia.

Treatment.—Treatment in the past has been limited to therapy of the masculinization in those patients who have survived infancy. With the recent work on the adrenal cortical hormones new hope can be offered these patients, and in the past five years encouraging reports in small numbers are being published.

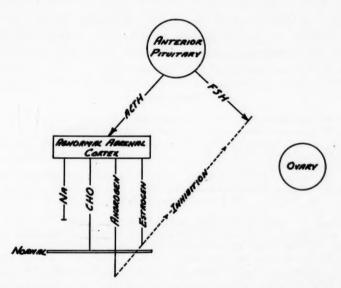


Fig. 4.—The mechanism of action of the abnormal hormonal stimulation as envisioned by Wilkins and co-workers.<sup>13</sup> ACTH is normal but in acting on an abnormal adrenal cortex produces an excess of androgens which in turn inhibit estrogens and FSH.

Wilkins and associates,<sup>13</sup> envision the mechanism of the disease as a normal stimulation of an abnormal cortex with subsequent overproduction of androgens and inhibition of estrogens through the medium of FSH (Fig. 4). Mazursky and Sawan,<sup>2</sup> Lewis, Klein, and Wilkins,<sup>3</sup> and Panos<sup>5</sup> have all reported good results in patients treated with desoxycorticosterone acetate and salt. DOCA in doses of 2.5 mg. and salt to 5 Gm. a day were the average doses used and in the two cases treated by Panos it was possible to discontinue the treatment with DOCA and maintain the patients on salt alone after one year.

The second facet of the problem is that of overcoming the masculinization and allowing these infants the opportunity for normal psychosomatosexual development. Wilkins and his group<sup>13, 14</sup> in the treatment of adrenal intersex with cortisone have shown results ranging from good to spectacular in causing regression of masculinizing traits. This work has been confirmed by Evans and Riley,<sup>15</sup> Taylor,<sup>16</sup> Vines and Dods,<sup>17</sup> and others.

In general, many other methods have been tried with equivocal results. Among these might be mentioned adrenal resection, estrogens, irradiation of the adrenals, surgical methods aimed at feminizing the genitals, and various combinations of these methods.

# Conclusions

The problem of adrenogenital virilism with hypoadrenia is admittedly a rare one, but not so rare that it may not be encountered by all of us at some time in our practice. We must be alert to recognize it, since the modern knowledge of the function of the adrenal gland gives hope for the treatment of these patients. The following points might be listed purely as emphasis: (1) In the child with a genital anomaly who presents a feeding problem, suspect the presence of the syndrome. (2) Confirm it with complete serum sodium, chloride, potassium, and nonprotein nitrogen studies, and, where possible, with analysis of 17-ketosteroid output. (3) Lifesaving treatment consists of desoxycorticosterone acetate and salt. (4) The use of cortisone may allow the normal development of the female infant.

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4301 MAIN STREET

# Discussion

DR. W. F. MANLY, Denver, Colo.—Dr. Keeler has added three cases to the growing list of a newly recognized clinical entity-adrenal cortical dysfunction. He is to be complimented on his paper and presentation and especially on the thoroughness of the case workups, two of which occurred in a period during which knowledge of adrenal corticoids was scant.

The cases presented all fall into the group of adrenogenital virilism associated with electrolyte imbalance. These cases represent dysfunction of not one but two of the layers of the adrenal cortex, namely, the glomerular and the reticular zones. Dr. Keeler mentions the speculation that the various zones are responsible for different functions. The glomerular zone supposedly regulates water and electrolyte balance. The fasciculata secretes the glucocorticoids such as cortisone. The reticulum produces the androgenic substances. This theory has received considerable support by the as yet unpublished work

of Jones and Jones in Baltimore. These investigators are using new histochemical techniques to demonstrate lipid material. In autopsy material of cases with this type of adrenal cortical dysfunction, there was a constant finding of hyperfunction of the reticular zone and hypofunction of the fasciculata zone. The same investigators have offered a clinical classification of this entity. It is as follows:

I. Female pseudohermaphroditism due to congenital adrenal hyperplasia.

This is characterized by virilism, possible hirsutism, malformations of genitals, and short stature due to early epiphyseal closure. The 17-ketosteroids are elevated.

Ia. Above plus abnormal electrolyte balance. Subgroup Ia is the above group plus electrolyte imbalance reflecting a disturbance in the glomerular zone. It is in this group that Dr. Keeler's three cases fall.

II. Postnatal virilism due to adrenal hyperplasia.

This group manifests the symptoms of virilism plus failure to begin menstruation, failure of puberty, and elevation of 17-ketosteroids. Genital anomalies are less severe.

III. Postpubertal hirsutism, oligomenorrhea, and infertility with elevated urinary 17-ketosteroids.

This group has no major abnormalities of the genital tract except possible enlargement of the clitoris. The menstrual interval is often prolonged and is anovulatory or associated with poor luteal function. Infertility is frequent and the 17-ketosteroids are usually mildly elevated.

IV. Postpubertal hirsutism, oligomenorrhea, and infertility with normal urinary 17-ketosteroids.

This group is the same as III except that the 17-ketosteroids are not elevated.

In Groups I and II the treatment is both surgical and hormonal. In the cases of electrolyte imbalance, such as presented by Dr. Keeler, adequate treatment is lifesaving. The surgical management is relatively easy with extirpation of the clitoris and perineoplasty. Treatment with cortisone suppresses the excessive ACTH stimulation to the reticular zone with a resultant fall in 17-ketosteroids and reversal of virilism.

Groups III and IV represent patients with probable adrenal hyperplasia developed later in life. After treatment with cortisone pregnancy occurred in 12 of 21 cases reported by Jones. Roughly 50 per cent of these aborted, however. At the University of Colorado Medical Center 9 cases falling into Groups III and IV have been observed for the past year. Cortisone treatment has produced bleeding in 4 of these amenorrheic women, none of it being of ovulatory character. No pregnancies have occurred. Treatment has been oral, cortisone in 50 to 100 mg. daily doses. If the 17-ketosteroids were elevated they promptly returned to normal levels. Signs of virilism were reduced or reversed. Continued observation of these cases under cortisone therapy must be maintained so that undesirable changes in metabolism do not result in a condition like Cushing's syndrome. The information available at present indicates that cortisone therapy must be maintained indefinitely and that adrenal atrophy probably does not occur from this treatment. Cortisone therapy represents a distinct advance in our gynecologic treatment and offers for the first time relief for these distressed individuals.

# THE REPEAT CESAREAN SECTION\*

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A SLOW, steady increase in the incidence of cesarean section has taken place in virtually all obstetrical centers. 6, 14, 20, 24 The greater number of births throughout our country, plus the increase in the use of cesarean section, places a larger number of our women in the classification, "previous cesarean section." The management of these sectioned individuals in future pregnancies becomes more and more of a common problem for our consideration.

TABLE I. STATE OF ILLINOIS, 1953

Total deliveries	197,458	
Cesarean sections	7,097	
Incidence	,	3.59%
Maternal deaths	63	
Associated with cesarean section	12	
Deaths in repeat cesarean section (all elective) 1. Anesthetic death (general)	3	
2. Anesthetic death (spinal) 3. Sepsis		

In the early years of this century, rupture of the uterus, with certain fetal death and too often maternal death, was not uncommon during labor in women with uterine scars. This danger led to the dictum, "Once a section always a section." As surgical techniques and postoperative management improved, rupture of the uterus in a subsequent pregnancy became somewhat of a rarity.

A few daring individuals noted that some patients scheduled for repeat section managed not only to go into labor of their own accord but often delivered rather easily and rapidly.

Many reports have been presented on this question of vaginal delivery following previous cesarean section, and comparisons have been made with patients who have been repeatedly sectioned.<sup>1, 3, 7, 9, 11, 16, 17, 22</sup> It has been shown that under proper circumstances vaginal delivery is safe, and some say the safer of the two procedures.<sup>3, 16, 17</sup> Schmitz<sup>17</sup> has changed the dictum to, "Once a section, not necessarily always a section."

Yet any study of cesarean section surveys will show the popularity of the repeat operation, especially in the management of private patients.<sup>2, 4, 5, 14, 15, 20, 24, 25</sup>

What, then, are the results to be obtained if one still follows the dictum, "Once a section always a section"? What are the hazards presented by this practice? In the light of present-day surgical techniques and auxiliary aids, are the results sufficient to continue to observe this principle?

<sup>\*</sup>Presented at the Twenty-second Annual Meeting of the Central Association of Obstetricians and Gynecologists, St. Louis, Mo., Oct. 7 to 9, 1954.

We must also keep in mind that there will always be a rather large group of patients in whom the indication for the primary abdominal delivery will persist, and a repeat cesarean section will be mandatory.

Since the incidence of the repeat procedure has become the chief indication for cesarean section, it behooves all of us to restudy our repeat sections, not only to see what we are accomplishing, but where we can improve our results.

TABLE II. FREQUENCY OF PREVIOUS CESAREAN SECTION AS THE INDICATION FOR CESAREAN SECTION IN RECENT SURVEYS

AUTHOR	YEAR	FREQUENCY (%)	
1. Verch	1950	 43*	
2. D'Esopo	1951	12	
3. Cody	1951	32	
4. Zarou	1952	31*	
5. Diddle	1952	28	
6. Zettleman	1953	37*	
7. Schaefer	1953	40*	
8. Posner	1954	27*	
9. Wolff	1954	42*	
Average	η	 30	

<sup>\*</sup>Leading indication for cesarean section.

### Material

This report is a study of 200 consecutive repeat cesarean sections on private patients. In the absence of complicating factors, repeat section was scheduled ten to fourteen days before term. The term was determined from the menstrual history, repeated prenatal examinations, and x-ray studies of fetal development at the estimated seventh month and again close to term. The date of surgery was based on the clinical judgment derived from these considerations.

TABLE III. HENROTIN HOSPITAL, CHICAGO, 1944-1954

Primary cesarean sections		266	
Repeat cesarean sections		200	
Elective	162		
Emergency	38		
Onset of labor	30		
Placenta previa	4		
Abruptio placentae	3		
Toxemia	1		

In the elective cases, hospitalization was on the day preceding operation. Physical examination and blood studies were carried out at this time. Surgery was performed in the early morning. The only preparatory medication consisted of evening sedation, mild enema in the morning, and atropine, 1/150 grain, before operation if a general anesthetic was to be given.

Anesthesia depended on the psychological reaction of the patient, and the availability of a competent anesthesiologist. It included local infiltration of 1 per cent procaine (usually with hyaluronidase), spinal, and general inhalation techniques. Local infiltration, often followed after the birth of the baby by Pentothal sodium intravenously, or inhalant gases, has constantly remained the most popular method. Spinal anesthesia has been used increasingly in the last few years. Ergotrate, ½320 grain, and morphine sulfate, ½ grain, are usually given intramuscularly as soon as the baby is born.

The low cervical operation was used in all but 8 patients. In 5, adhesions and the presence of the bladder high on the uterus made the classical procedure the one of choice. Cesarean hysterectomy was performed twice, once for associated large uterine fibroids and once for severe uterine bleeding at the time of operation. The one Norton extraperitoneal operation was elected so that the surgeon could become acquainted with the technical details in a simple case.

One hundred sixty-seven of these operations were the patients' second cesarean sections, twenty-eight were the third, four the fourth, and one the fifth

Sterilization procedures (other than hysterectomy) were carried out on 42 patients. Twenty-three were done at the time of the second section, 17 at the third, and 2 at the fourth. The Madlener and Pomeroy techniques were the most popular. Sterilization was necessitated by medical contraindications to future pregnancies in 4 patients (2 hypertension, one heart disease, one tuberculosis). Sterilization was routinely suggested at the time of the second section and demanded at the third. Unfortunately, the babies of two mothers who were sterilized at the second section died of neonatal atelectasis.

The baby is cared for by a resident or obstetrical colleague. An incubator is preheated and prehumidified. Oxygen and tracheal catheters are ready if needed.

Postcesarean puerperal care simulates that of the postoperative gynecologic patient. An indwelling catheter inserted into the bladder before surgery is usually left in place for several hours and then removed. Sedation and pain relief are offered during the first twenty-four hours. Early ambulation is encouraged. Fluids and food are given as welcomed by the patient. The hospital stay is eight to ten days.

This planned program is often interrupted by the circumstances of complications of pregnancy. In these 200 patients, the elective procedure was followed in 162. Emergency cesarean sections were performed in 38. In this latter group, 30 began labor before the planned date. Placenta previa complicated the pregnancy and demanded operative interference in 4 patients, while premature separation of the placenta similarly developed in 3. In one patient a severe toxemia forced an early delivery.

### Maternal Mortality

There were no deaths in this series. Lest we become too complacent, we must be constantly reminded of a maternal death in our hospital in 1938. This patient, aged 36, had an elective repeat (second) cesarean section at the thirty-ninth week of pregnancy. It was done under local infiltration (1 per cent procaine) anesthesia. Surgery was simple and a low cervical section, with delivery of a 9 pound baby, was readily accomplished. Wound separation with complete evisceration and protrusion of the bowel through the abdominal opening developed suddenly on the sixth postoperative day. In spite of an immediate surgical repair, a severe sepsis took place. Peritonitis, followed by endocarditis, pericarditis, and pneumonia, led to death on the twenty-second postoperative day. (This was the only death following cesarean section since the hospital was opened in 1935.)

There were 3 maternal deaths in the State of Illinois during 1953 in patients who underwent elective cesarean section. One was due to a prolonged sepsis. Two of the deaths occurred in the operating room. Both appeared to be due to the anesthetic (one, general; one, spinal).

# Maternal Complications

Complications Encountered at Surgery .-

Adhesions between the parietal peritoneum and the visceral peritoneum in the region of the uterovesical fold are not uncommon. They tend to draw the bladder well up above the symphysis. It is often in the line of incision. Caution in entering the abdominal cavity will prevent bladder trauma. This also holds true in attempting to free the bladder from the uterus to expose the lower uterine segment. The 5 classical cesarean sections in this series were done because of these adhesions and the high location of the bladder. Nevertheless, the bladder was traumatized during 4 low cervical cesarean sections. Surgical care, plus a retention catheter left in the bladder for seven days, was followed by spontaneous healing. These cases all occurred in the elective group of sections.

Bleeding during cesarean section is often more severe than it should be. In a study of the blood findings in 100 patients on the fourth day following section (previously reported), 30 per cent were anemic (erythrocytes less than 3.5 million and/or hemoglobin below 10 Gm. per 100 ml. of blood). There was no difference between the elective and the emergency cesarean groups.

Other surgical problems are difficult to evaluate because they are not well expressed on the records by the operating surgeons. It was noted that in this group the usual (mean) operating time was fifty-five minutes from the start of the anesthesia to the last skin suture. The experiences of the obstetricians in this group may be further shown by the fact that the operating time was less than forty minutes in 42 cases (22 per cent). (No one hurries his surgery, yet puttering is a bad policy.) In 17 per cent (34 cases) it took the same surgeons more than one and one-half hours to complete the operation.

Complications Post Partum.—

Postpartum hemorrhage: Attention to surgical details, correct management of the third stage of labor, thorough inspection of the placental site, and attention to enhancing uterine contractions during surgery should prevent severe bleeding. Yet, there were 5 cases of postpartum hemorrhage. In one patient, bleeding and uterine relaxation were so severe that a hysterectomy became necessary.

Pelvic hematomas: A large hematoma developed in one case—so large an accumulation that four blood transfusions and a twenty-five-day postoperative hospital stay were needed before improvement took place. Fourteen other patients developed small indurated areas in the region of the peritoneal flap. These were gradually absorbed. They caused only minor discomfort and were interpreted to be hematomas. They were distributed somewhat evenly between the two groups of sections. Seven had a short febrile course.

Fever of 100.4° F. or higher for forty-eight hours excluding the first twenty-four hours developed in 25 patients (12.5 per cent). In 5 it was associated with urinary tract infections. Pneumonia (aspiration) was noted in one patient. Thrombophlebitis was severe in one patient. Nine had fever of undetermined origin. All recovered. Acute mastitis occurred in one patient and healed by resolution. Wound evisceration and pelvic hematomas accounted for the remainder.

Evisceration: Complete wound separation took place in 2 patients on the fifth and seventh postoperative days, respectively. Immediate surgical repair was followed by recovery.

Normal uneventful afebrile recoveries took place in 168 mothers (84 per cent).

TABLE IV. POSTOPERATIVE COURSE

Normal uneventful recovery		168	
Morbidity		25	
Pelvic cellulitis with small hematoma	7		
Urinary tract infection	5		
Pneumonia	1		
Thrombophlebitis	1		
Large pelvic hematoma	1		
Acute mastitis	1		
Fever (origin obscure)	9		
Postpartum hemorrhage		5	
Postpartum anemia (100 cases)		30%	
Evisceration		2	
Bladder trauma at surgery		4	
Small pelvic hematoma		14	

# Infant Mortality

There were 5 infant deaths in the group (2.5 per cent). Four were neonatal deaths. The one stillbirth was due to severe placental separation that came on in the thirty-fifth week of pregnancy. One of the neonatal deaths followed section for placenta previa at the twenty-eighth week. The baby weighed 1 pound, 12 ounces, and lived thirty hours.

Three infant deaths followed elective sections performed at term. All were due to anoxia at birth followed by atelectasis. Two infants weighed slightly over 6 pounds, the third weighed 5 pounds, 13 ounces. All 3 mothers received general anesthesia for the surgery.

TABLE V. INFANT MORTALITY

Neonatal		4	
Elective section	3		
Placenta previa	1		
Stillbirth		1	
Abruptio placentae	1		

# Infant Morbidity

Delay in initial respiration with resultant anoxia occurred in 8 infants. This was severe enough to require resuscitation and continual oxygen administration for several hours. All recovered. All were in the elective cesarean group. All 8 mothers were sectioned under general anesthesia.

Atelectasis developed shortly after birth in 10 other infants. Nine mothers received general anesthesia before the birth of the babies. Local anesthesia was used in one case.

Severe *cerebral irritation* as shown by marked tremors and mild convulsions were present in 2 cases. One mother received general anesthesia and one spinal anesthesia. Both were in the elective operative group.

TABLE VI. INFANT MORBIDITY

Elective cesarean section		17	
Anoxia, general anesthetic	8		
Atelectasis, general anesthetic	5		
Atelectasis, local anesthetic	2		
Cerebral irritation, general anesthetic	1		
Cerebral irritation, spinal anesthetic	1		
Emergency		3	
Atelectasis	3		

# Prematurity

Forty-four infants (22 per cent) weighed less than 6 pounds at birth. Weight Less Than 5 Pounds.—

There were 12 infants in this weight class (6 per cent). Two of the mothers were electively sectioned at the supposed thirty-eighth week of pregnancy. One infant delivered under general anesthesia was anoxic at birth. At lectasis followed. Oxygen was needed for thirteen days. The baby weighed 4 pounds, 7½ ounces. It remained in the hospital for twenty-five days. This baby has developed definite manifestations of cerebral palsy. A second infant, so delivered but under local anesthesia, weighed 4 pounds, 13 ounces, did well from birth, and is in good health today.

There were two sets of twins; the mothers both went into labor at the thirty-sixth week of pregnancy. Local anesthesia was used at delivery. The babies weighed 4½ pounds each in one set, and 3 pounds, 14 ounces, and 3 pounds, 15 ounces in the other set. All have developed well.

Two mothers went into premature labor, both at the thirty-fifth week. A 3 pound, 15½ ounce infant was delivered under a general anesthetic; it was anoxic at birth but recovered. The second was a 4 pound, 11 ounce infant. This delivery was aided by local anesthesia. The baby was in good condition at birth and has remained healthy.

Placenta previa with severe bleeding was the indication in 2 mothers. One baby born at the twenty-eighth week weighed only 1 pound, 12 ounces, and lived only two days. The second infant was delivered under general anesthesia at the thirty-ninth week. It weighed 4 pounds, 14 ounces, and is in good health.

One mother scheduled for a repeat section developed severe abruptio placenta at the twenty-eighth week. The fetal heart rate was grossly irregular. Immediate section was done with local anesthesia, and a 2 pound, 8 ounce baby delivered. It was in surprisingly good health and has grown nicely.

A 3 pound, 9 ounce infant was delivered with local anesthesia at the thirty-fourth week when the mother's blood pressure rose to 206/108 and symptoms of severe pre-eclampsia developed. The baby is in good health today.

TABLE VII. PREMATURITY

Infants below 6 pounds' birth weight	44	
Infants below 5 pounds	12	
Elective	2	
Emergency	10	
Infants between 5 and 6 pounds	32	-
Elective	25	
Emergency	7	

Weight Less Than 6 Pounds but Over 5 Pounds .-

Thirty-two infants were in this weight class. Twenty-five of these infants were delivered at term via elective cesarean section. One infant (delivered with general anesthesia) died. This case has been reported. Two were anoxic at birth. One, delivered under local anesthesia, recovered promptly. The second, delivered under general anesthesia, was anoxic, became atelectatic, was ill for eight days, and recovered. Twenty-one were normal at birth. Fourteen were delivered with general anesthesia and 7 under local (2 spinal).

Emergency cesarean sections were necessary in 7 of this weight class due to the onset of labor, one due to abruptio placentae, and one due to recurrent toxemia. All infants were born in good condition. Five of the mothers received local anesthesia, and 2 received general.

# Anesthesia

Local infiltration anesthesia, often followed by either intravenous Pentothal or inhalant gases after the birth of the baby, was used in 92 patients.

General inhalation anesthesia (nitrous oxide-cyclopropane, ethylene, ether) was equally popular and was used in 90 cases. Spinal anesthesia was used only 18 times.

The relationship between the anesthesia and infant respiratory difficulties has been noted under infant morbidity.

### Comment

A rapid glance at the statistics here presented would lead one to think that the repeat cesarean operation is a safe and simple solution for the mother and hazardous only for the baby, due to poor timing of the date of elective surgery. The fact that the entire surgical and recovery course was normal and uneventful in 168 out of 200 patients (84 per cent) would lead one to this conclusion. The absence of maternal deaths or stormy postoperative phases tend to support this thesis.

Yet we must recognize that the same hazards exist in respect to cesarean section as to any surgical procedure. Whenever we take a woman into the operating room for an abdominal operation, we immediately expose her to the dangerous complications of anesthesia, surgical accidents, infection, thromboembolic phenomena, and in this instance the complications of pregnancy such as hemorrhage and pelvic infection.

To avoid these complications and to see that every patient who enters the operating theater for elective surgery makes a good recovery, we should analyze our results in an objective manner. By so doing, we can see where we as individuals can improve our surgical technique, our judgment, and our attention to the details of postoperative care.

In this series, injury to the bladder at surgery and postoperative urinary tract infections were too common. Knowledge of the position of the bladder in relation to the lower uterine segment is important. Extension of the uterine incision into the upper uterine segment is better than undue dissection of the bladder area. We must pay more attention to the early signs of urinary tract infection so that early treatment can be instituted.

Hematomas beneath the uterovesical peritoneal flap or within the broad ligament should be prevented by adequate hemostasis at the time of surgery. Perhaps we hurry too much, especially to close the abdominal wall before making a complete and thorough inspection of the operative site to be certain it is dry.

Have antibiotics made us less alert to the prevention of infection? We must be more concerned with keeping bacteria out than the present, simple means of attacking them later. Vigilant attention to aseptic details is still fundamental in practice as well as theory.

Difficulties at surgery—operations lasting over an hour and one-half—mean either poor teamwork or difficult problems arising at the time of opera-

tion. Adhesions can make any procedure time consuming. Perhaps we should be more gentle and more aseptic when we do the first section. Maybe we would not see these adhesions at the second.

The incision into the uterus should be adequate enough to permit an easy delivery of the baby. Often it is not, and the surgeon makes this simple problem a difficult one. In attempting to deliver the baby through a small uterine incision, he will tear the uterine muscle and fibrous tissue. Not only will large venous sinuses be torn and bleed profusely, but healing of this torn area will be poor and lead to a weak scar.

Suturing of the abdominal wall must always be careful and correct. The two eviscerations in this series are two too many. Early ambulation causes a strain on the abdominal wound. You will soon note your surgical deficiencies by the number of wound complications in today's patients.

Too many of our patients were anemic following an elective cesarean section. Accurate blood study before section is certainly important; and so is the presence of a pint of blood at the time of operation. But most important of all are the conservation of blood and the prevention of blood loss while operating. Likewise, the correct management of the third stage of labor is just as important at cesarean section as it is following vaginal delivery.

It is agreed that the baby is not immune to the dangers of an elective repeat cesarean section.<sup>5, 10, 12, 13, 18, 19, 21, 22</sup> Three neonatal deaths should not have occurred. Most of the anoxic babies and those who developed at electasis should have been breathing at birth. Mack<sup>13</sup> has pointed out the increased death rate in babies born by section compared to vaginal delivery and noted that at electasis accounts for one-third of the deaths. Diddle<sup>5</sup> feels these deaths are due to poor timing of the date of surgery. Taylor<sup>19</sup> states that the factor of the weight of the baby is most important. Certainly we failed to select the proper date for surgery in too many instances. We tend to point with pride to the absence of rupture of the uterus, not only in this series, but in our hospital in general. Yet our elective repeat cesarean babies are too small. We need better methods of determining fetal maturity, size, and development. We must improve our judgment in this capacity.

We feel that anesthesia plays an extremely important role in both maternal and infant complications. General anesthesia is fine for the psychological appeasement of the mother, but is it physiologically the best for her and for her newborn? Retching and vomiting, a common part of the awakening period, do not do the sutured tissues any good. Small peritoneal tears and hematomas might get their start at this time. Why were almost all of our anoxic and atelectatic infants in the group whose mothers received general anesthesia? Should we not utilize local anesthesia to a greater extent? What about the place of spinal anesthesia in elective repeat cesarean section?

The emergency repeat cesarean section by its emergency nature adds to the dangers just mentioned. Our first duty is so to organize our hospital staff that the emergency is taken in stride. The accidents of pregnancy, such as placenta previa, abruptio, etc., must be cared for at once, and each case must be treated in an individual fashion. When a patient scheduled for an elective cesarean section goes into labor or the membranes rupture, would it not be better to evaluate her status carefully rather than rush into an emergency abdominal delivery? Perhaps we have erred in this by not permitting a trial of labor and an attempt at vaginal delivery.

Sterilization in itself is a most serious procedure and one not to be undertaken lightly. The present-day incidence of uterine rupture is extremely low. Should we not re-evaluate our thoughts regarding mandatory sterilization at the second or third cesarean operation? Should we not sterilize only on the grounds of medical contraindication to future pregnancies and individualize the obstetrical indication, based on the appearance of the uterus as seen at the time of surgery?

Since anoxia and atelectasis are so common, adequate care of the newborn becomes a necessity. An experienced clinician should be in attendance for the baby at every cesarean section. We should not pass on this duty to an intern or nurse. Care of the newborn involves more than tying of the cord and care of the eyes. The newborn infant's physician should have all the means for providing this service at hand. A warm incubator and a good supply of oxygen are essential. Facilities for blood counting, blood smears, and Coombs tests should be available. Gastric suction has been recommended. Most important is intelligent observation. We must watch these babies carefully for several hours. Immediate treatment of anoxia and atelectasis by accepted methods will bring about successful results.

Following the completion of the operation, we are in too great a hurry to move our patient to her room. It would be fine if each hospital had an obstetrical recovery room. In the absence of this, we should make the operating room a recovery room. Close observation in the immediate postoperative period will detect the major complications of shock and hemorrhage, will prevent post-anesthetic accidents, and will discover the postpartum bleeding of an atonic uterus. Then we can transfer her to her lying-in room under pleasant circumstances.

#### Conclusions

The increasing incidence of cesarean section in general and the repeat cesarean section in particular is noted.

Repeat cesarean section by its surgical nature subjects the mother to the inherent dangers of a major surgical procedure. Complications referable to anesthesia, surgical difficulties, infection, and to the postoperative period can and do occur. The hazards of pregnancy are added to this.

Prematurity in the infant is an all too common occurrence in this elective type of delivery. Accurate determination of the date for elective section is necessary to avoid delivery of premature and small babies.

Respiratory difficulties of the newborn appear to be related to both the small size of the infants and the use of general anesthesia at delivery.

Two hundred cases of repeat cesarean section have been reviewed and the results reported. There were no maternal deaths. There were five fetal deaths.

Improvements in surgical technique and better postoperative care will prevent complications. The choice of anesthesia is extremely important. Care of the newborn is an important clinical problem.

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#### Discussion

DR. CHARLES J. SMITH, Chicago, Ill.—It is of considerable interest to note that, as medical science progresses, the arbitrary termination of a woman's reproductive capacity is less and less tolerated, both by the patient and the profession. We may some day hope to see the time when the so-called medical indications for sterilization or abortion are abolished by the improvement of professional care in these medical problems.

The question of the integrity of the uterine scar with the potential hazard of rupture has by this time, we believe, been relegated to its proper status. Both in studies such as Dr. Wolff's and those of ours to establish the validity of vaginal delivery following cesarean section, the scarred uterus has demonstrated a marked capacity to tolerate the strain of gestation as well as labor. This seems to apply whether the uterus has been opened once or several times.

As Dr. Wolff points out, the "previously sectioned patient" is becoming more and more prevalent. He asks a number of pertinent questions, the answers to which should enable the qualified obstetrician to undertake the case of the highly fertile, previously sectioned patient with equanimity.

Through the courtesy of Dr. James Bremner, who studied the question of multiple cesarean sections at St. Francis Hospital in Evanston, Illinois, and on our service at Lewis Memorial Maternity Hospital, we have 105 cases available for study. None of these patients had less than three cesarean sections and one had seven. There were no maternal deaths and there was a 14 per cent incidence of postoperative morbidity. In three of the cases the old scar was found to be thin or with some dehiscence. There were twenty cases in which adhesions were found. In all the others the findings were unremarkable. In the light of Dr. Wolff's experience and our own, these 305 cases would demonstrate that no arbitrary limit to the number of cesarean sections can be established. Elective sterilization does not seem to be a valid procedure simply because the patient has been sectioned before. The hazards that the patient is subjected to seem to be no greater at the sixth section than at the first.

Dr. Wolff does well to emphasize the influence of the length of gestation on fetal outcome. Elective cesarean sections are notorious for producing premature babies and the establishment of a date for surgery should be less determined by the calendar than by clinical judgment. The essayist has shown, however, that despite all precaution it is still very easy to operate too soon.

The authors have undertaken the study of a question which by virtue of a lack of statistical evidence tends to be controversial. Although their figures would support an affirmative stand, they seem reluctant to take it. It is hoped that further tabulation of these cases may enable all of us to reject the unhappy procedure of limiting woman's greatest function.

DR. A. W. DIDDLE, Knoxville, Tenn.—Prior to 1944 maternal infection was commonly the determining factor as to whether or not abdominal delivery was done. Even if vaginal delivery might entail unusual maternal trauma and fetal risk, it was felt the mother could usually have another pregnancy after an unfavorable vaginal delivery with less hazard than if she became pregnant again after section. Subsequent to 1944 the availability of blood banks, better anesthesia, antibiotics, and chemotherapy made section a safer and more elective procedure. Consequently emphasis has swung away from maternal to fetal mortality. Several surveys in recent years confirm the opinion that fetal mortality is considerably higher with section than the rate for all deliveries. Part of the fetal loss is attributable to the complication for which the operation was done. On the other hand, much is due to poor timing or selection of section on the basis of unjustifiable indications.

For example, 1,312 women were treated by abdominal hysterotomy with delivery of 1,327 babies in a four-year interval ending Jan. 1, 1953, in the area of Knoxville, Tennessee. One hundred twenty-six, or 9.5 per cent, of the babies were either stillborn or died neonatally. The mortality rate among 894 babies born by primary section was 10 per cent (93 cases). Over half of the primary sections associated with fetal death were considered unjustifiable for both maternal and fetal reasons. In contrast, 7.6 per cent (33 cases) of 433 infants delivered by repeat section were lost. More than 11 per cent of the 433 babies weighed less than 2,500 grams. A majority of the babies that died were premature. Fetal wastage was usually associated with uterine rupture or poor timing of the cesarean section. The mortality and prematurity rates were nearly double the rates for all deliveries in the same period of time (Am. J. Obst. & Gynec. 63: 967, 1952; Am. Pract. 5: 216, 1954).

Twelve of the 428 women (3 per cent) subjected to repeat section suffered uterine rupture. One died and the other 11 survived. Three others had intestinal obstruction postoperatively. These obstructions proved to be consequences of the first laparotomy. This was the experience in only one of the six hospitals surveyed. Whether or not additional instances of this complication were seen in the other five is unknown.

The results recited tell a story. First, too often we lose sight of the fact that errors in judgment may be perpetuated once a patient is sectioned. A section makes a woman, to some degree at least, a reproductive cripple. It is to be understood that there is no opposition to the use of the procedure when indications are proper. To the contrary, the purpose is to emphasive that there is a definite potential maternal morbidity and mortality rate associated with the procedure. Second, a favorable fetal salvage rate, where the indication for operation is previous hysterotomy, requires careful timing of the section.

DR. C. W. SEIBERT, Waterloo, Iowa.—To me, the big problem is the time for operation. In the past I think it has too often been customary to schedule a woman for repeat cesarean section, two weeks prior to the expected date of confinement. Too often I have

been embarrassed by having too small a baby, and, personally, I no longer schedule these women until at least their due date, and that must coincide with clinical judgment. Now and then you have to get up at midnight to operate, because the patient goes into labor, but I have found that you are much less often embarrassed.

DR. WILLIAM J. DIECKMANN, Chicago, Ill.—Here are 200 elective repeat cesarean sections, presumably by experts, which should ensure a live mother and a live baby. Fortunately, they had no maternal deaths. That is not the usual course of events, and I am sure that, in a larger series, sooner or later there will be a death from anesthesia or from embolism. Dr. Wolff reported 2 deaths from anesthesia in elective cesarean sections in Illinois, and 1 from sepsis.

So far as the mother is concerned, I think you should be prepared to use one or two of the four types of anesthesia—inhalation, spinal, local, and intravenous. Somebody in the hospital should be competent to administer one, two, three, or if necessary, all four of these various types of anesthesia, because sooner or later they will not be able to perform a spinal, or the lungs may be wet and you cannot give an inhalation anesthetic.

I favor local anesthesia, primarily in the interests of the baby.

The authors report a 2.5 per cent perinatal mortality in repeat cesarean sections.

One of the other discussants suggested that perhaps it was better to let these patients go to term, or actually go into labor. We tried that, but recently had an aspiration death in a breech delivery, so that gave us cause for a review, and for some time now I have been sending these patients in for repeat section when there is some beginning of cervical dilatation. I disregard the menstrual age.

In addition, we are dehydrating these patients for at least 24 hours by limiting their fluids, using ammonium chloride or a diuretic.

In the last 18 months we had 45 consecutive elective cesarean sections on my service, in some of which the indication was toxemia, and in which no baby died from hyaline membrane or atelectasis.

DR. JOSEPH E. KOPCHA, Gary, Ind.—Well, it gladdened my heart to see that we, as leaders of our country, are at least sticking to the dictum, "Once a section, always a section."

Remember that the general practitioners are looking to us to lead them on to what we think is the best method of treating these patients. Remember that we are speaking in terms not of the teaching centers but far out in the suburbs and in smaller cities where we are not close to the teaching centers.

I also deplore the articles that appear now and then in the literature on how many patients have had vaginal deliveries who had had repeat sections. Well, it's fine for the doctor to take a chance, but actually, is the doctor taking the chance? It is the patient who is taking the chance, and when she is buried six feet under the ground with a ruptured uterus, it makes a difference. I think the authors should be commended on their splendid work, and I hope we stick to our dictum, "Once a section, always a section."

DR. CARROLL J. FAIRO, Cincinnati, Ohio.—Dr. Wolff mentioned a vertical incision. He also mentioned that the bladder was higher. Am I right or wrong, Dr. Wolff, that you were actually doing a low classical?

Also, am I right or am I wrong that in the low cervical cesarean it would be possible to deliver some of these women later without a repeat section, except for disproportion, and so forth? I may be wrong, but as I recall, there was some discussion that the scars of the low section would not rupture as easily as the scars of the classical.

I would like to ask Dr. Wolff if he has done any vaginal deliveries after a section—of course, disregarding cases of disproportion.

The last question concerns anesthesia. I notice you did 923 cases under local. What have you against spinal, or low saddle block? In my hands (and I have tried it many

times), local anesthesia is actually more vocal than it is local. I have seen many men do this operation under local anesthesia, and I find that most of them are vocal, also. So I would rather use spinal.

I wish to ask Dr. Wolff about his time element—55 minutes. Do you mean, Dr. Wolff, from the time of your incision, or do you mean the time you start the local anesthetic?

I wish to ask what your results are with local anesthesia. Do you give the anesthesia when the patitent lies quietly there, or is she talking, and saying, "It hurts, Doctor," and you say, "I'll put in a little more medicine," and that conversation goes on through the entire operation? At least that is what happens in my hands.

I would like to learn from you this morning how to do this operation. In our town we have all tried local anesthesia, but we have practically all given it up. A good many of our men were trained in Chicago, and they have given it up. I wish Dr. Wolff would tell me what he does. Is it more vocal or is it more local?

DR. JOSEPH W. KELSO, Oklahoma City, Okla.—I wish to ask the essayist whether he uses Novocain, and second, whether he has any knowledge of the circumstances of the deaths from spinal anesthesia in the state of Illinois. Was the anesthetic given by recognized anesthesiologists or by the attending physician himself?

DR. WOLFF (Closing).—The purpose of this report was to call your attention to a very common clinical problem which faces all of us. It was hoped that this report would elicit some discussion, and I am quite pleased that it has.

I will only answer one question, and that is one by Dr. Kelso. Yes, in answer to his question regarding the death from spinal anesthesia during a repeat cesarean section in the state of Illinois, an anesthesiologist gave the spinal anesthesia.

The many other questions that have been asked all deserve answers, but they are all problems that are common to everybody in this room. They are all matters of opinion, and I think it would be better to leave you with your own thoughts on them.

# USE OF CORTISONE IN THE PREVENTION OF ERYTHROBLASTOSIS IN INFANTS OF RH-SENSITIZED MOTHERS\*

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RIOR to the clinical inauguration of this study in August, 1951, extensive conferences were held in order to determine the feasibility of employing cortisone† to prevent the development of erythroblastosis in infants of pregnant women who were isoimmunized by the Rh factor.

From the very beginning it became apparent that multiple variants would present obstacles. The literature, at that moment, was filled with a multitude of small reports of isolated instances telling of both exuberant success and/or miserable failure in the use of cortisone in every conceivable facet of disease. Reports of untoward reactions further clouded the picture. There was, in addition, a dearth of information in regard to the effect of cortisone on pregnant women or their infants.

The final decision to employ cortisone was greatly influenced by the demonstration of the favorable action of ACTH and cortisone on other hematological entities, characterized by immunohumoral factors. For example, in acquired hemolytic anemia treated with corticotropin, there was reported a rapid change in the blood picture toward normal. Cortisone was felt to inhibit the hemolysis of the red blood cells affected. This line of thought was later incorporated in the reports of Hunter and Ross<sup>2, 3</sup> in evaluating a like study.

The personnel involved in conducting this study included Dyer and Smith, obstetricians, Dent, pediatrician and pediatric pathologist, Derbes, allergist, and Davenport, serologist. Only with the combined efforts of these individuals did it appear possible to attempt such a complex problem.

# The Problem of Rh Sensitivity

From our experiences as well as from the studies in the department at Tulane, 4, 5, 6, 7 the following findings have been relatively constant:

- 1. Fifteen to 17.7 per cent of white women are Rh negative, 4.5 to 8 per cent of Negro women are Rh negative (Table I).
- 2. Approximately 13 per cent of Rh-negative women are married to Rhnegative men (King's series of 1,000).

<sup>\*</sup>Presented at the Twenty-second Annual Meeting of the Central Association of Obstetricians and Gynecologists, St. Louis, Mo., Oct. 7 to 9, 1954.

†Cortisone (Cortone acetate, Merck) used in this study was made available through the cooperation of Merck and Co., Inc., Rahway, N. J.

- 3. In a study of 569 consecutive pregnancies of white patients (King and Davenport<sup>4</sup>), 1.05 per cent lost infants with hemolytic disease. In 1,000 patients this figure remained constant.
- 4. If the husband is homozygous the effect is theoretically constant. If he is heterozygous there is a theoretical reduction of 50 per cent.
- 5. Davenport has a strong belief that approximately one-third of Rhnegative human beings will not develop iso-immunization regardless of the circumstance of the contact with the Rh factor.
- 6. As small an amount as 0.1 c.c. of Rh-positive blood is enough to sensitize some individuals.
- 7. A primigravida without history of transfusion may be grossly sensitized by Rh-positive blood administered her (in the buttocks) as a newborn.
- 8. Definite prognosis cannot be made as to whether the infant will be affected or survive, even though the character, concentration, or type of antibodies found in the pregnant mother are known.
- 9. Whole families of Rh-negative women may produce offspring with no difficulty in regard to this problem while other families of sisters have readily become sensitized early in their reproductive careers.
- 10. Once a mother has produced an infant with the classical effects of Rh sensitivity, the chances are great that in subsequent pregnancies the infants will be equally affected and probably show greater depths of the hemolytic process.
- 11. No reduction of maternal or infant sensitivity was noted with the use of ethinvl disulfonate or with haptens.
- 12. Premature termination of pregnancy has not improved the fetal salvage. To the contrary, the prematurity thus induced complicates the management of an already complicated problem.
- 13. In seven years of searching for sensitization appearing at 6 weeks post partum in women who demonstrated no antibodies ante partum, we have yet to discover an instance. This includes all types of deliveries.

With this background of thought, cortisone was employed with the hope in mind that this agent would prevent the hemolytic process in the fetus in utero, or at least help produce an infant who could be salvaged.

TABLE I. INCIDENCE OF RH NEGATIVITY

RACE	NUMBER TESTED	PER CENT NEGATIVE REACTIONS	INCIDENCE OF ERYTHROBLASTOSIS FETALIS (PER CENT)
White (King & King)	1,000	17.7	1.05
Negro (Levine)	264	4.5	-
Negro (Landsteiner & Wiener)	113	8.0	0.7
Japanese	150	2.0	Very rare
Chinese	150	0.7	Very rare
American Indian	120	0.8	Very rare

#### Selection of Patients

Because of the experimental aspects of such an undertaking, screening of the patient was of importance. In the first place, we were forced to rely on white women from private practices of interested obstetricians in our vicinity. This problem is rare in the Negro race who furnish 80 per cent of the 12,000

deliveries per year at Charity Hospital in New Orleans.

From the start, it was apparent that little could be gained by merely treating any pregnant mother who developed or exhibited Rh antibodies in her blood. We had formed no method of correlating the serological blood picture with the prognosis of the infant. Therefore, it appeared to be of greater importance to treat only those women who had previously delivered infants with proved evidence of erythroblastosis. For comparison, five women who had not delivered affected babies previously were treated. In all, alarmingly high antibody titers were present.

This imposed certain difficulties in so wide a distribution of clinical material but these were coordinated by offering the services of the consultants mentioned, both during the course of pregnancy and at delivery. It also included pediatric care in the neonatal period.

Applications were received from the obstetricians of likely candidates and if they fell into the previously mentioned category they were accepted for the study. Initial chest x-ray surveys were conducted, followed by a blood survey. The latter included a complete blood picture, red cell count, white cell count, hemoglobin, hematocrit, differential, eosinophil count, and bleeding and coagulation times. In addition, the Rh, Hr determination, as well as antibody titer determinations, were performed.

TABLE II. UNTOWARD REACTIONS TO CORTISONE

I. Skin Changes.—	
Hirsutism	Keratosis pilaris
Loss of scalp hair	Pigmentation
Acne vulgaris	Urticaria
Striae	Purpuric tendencies
Thinning of skin	Painful nodules
II. Central Nervous System Changes	
Euphoria	Schizoid episodes
Optimism	Self-confidence
Insomnia	Increased physical activity
Garrulousness	Accelerated thinking
Giggling	Bulimia
Excitement	Apprehension
Phobias	Anxiety
Depression	Hypomania
III. General Changes.—	
Glycosuria	Nausea
Edema	Diarrhea
Hypertension	Decreased clotting time
Muscular weakness	0

Cortisone in oral doses of 25 mg. four times daily (total 100 mg. per day) was then begun, ideally, at the twenty-eighth week of gestation. The patient was instructed to adhere to a very strict low-salt diet, warned to report any untoward reactions, and was given weekly office appointments. On these visits a list of untoward reactions was reviewed (Table II). After the first two weeks of treatment potassium chloride, 1 Gm. daily, was added to the therapy to replace potassium loss when indicated. If any untoward reactions occurred, these were evaluated and if indicated the dose of cortisone was reduced and on some occasions it was discontinued for a week and then gradually resumed. Urinary albumin and sugar determinations were performed at each visit and the complete blood survey was repeated every two weeks.

# Management of the Infant

At delivery the umbilical cord was cut long (15 to 20 cm.) and a specimen of cord blood was obtained for study. In most instances a polyethylene catheter was inserted into the umbilical vein at birth. A peripheral blood study was also performed. The combination of both blood specimens was examined for hemoglobin levels, nucleated red blood cells, a total red cell count, Rh determination, a Coombs test, and, if indicated, an icterus index.

The infant received an immediate exchange transfusion if there was evidence of marked visceromegaly and/or clinical jaundice even before confirmatory laboratory reports were received. Other criteria for exchange transfusion included marked levels or combinations of bilirubin between 3 and 5 mg., icterus index in excess of 20 units, hemoglobin below 15 Gm., a red blood cell count of less than 4,000,000, and/or a continued increase of nucleated red blood cells.

All infants received penicillin in parenteral injections (20,000 U. aqueous every 4 hours). In the latter half of the study it was learned that there was no necessity to withdraw cortisone in the infant. Likewise in the latter two-thirds of the study no emphasis was placed on the use of Rh-negative female blood in transfusing the infants.

One early and relatively constant finding was the fact that erythroblastotic babies born of mothers who were taking cortisone usually looked well. Subsequent observations continued to demonstrate that cortisone masks the clinical appearance and delays, to some extent, the rapid development of jaundice seen in erythroblastosis fetalis. This particular finding lulled attending physicians on two separate occasions into a false sense of security and delayed positive treatment to the detriment of the infants.

Cortisone was administered to the mothers post partum and withdrawn over a period of seven days. Seventy-five milligrams was given the first day, 50 mg. the second and third days, and 25 mg. on the following four days. Follow-up studies were obtained on both mothers and babies for six months after delivery with the exception of the very recently completed cases.

## Effect of Cortisone on the Pregnant Woman

No untoward reactions were observed in 20 of 45 women treated (Table III). Generally speaking, most mothers admitted that they felt exhilarated while taking the drug, and many remarked jokingly that they wished the drug could have been continued post partum. In one particular instance an intelligent and most cooperative patient who tragically enough delivered a stillborn baby after 13 weeks of therapy remarked that the cortisone had made her feel so good, she did not mind so much losing this baby!

There were mild reactions in 22 women, the most common of which was moderate edema. Severe reactions occurred in three patients, namely, one mother exhibited acute acne, and her infant was born with an acneform eruption, one instance of severe nausea and headaches, and one psychotic episode requiring institutional care. The last mother was poorly selected and we concluded later that she should not have been a candidate for cortisone. The drug was withdrawn, and she carried her pregnancy to term, delivering a stillborn infant. Regardless of the character of untoward response, all reactions, with the exception of this psychosis, were immediately reversible upon withdrawal of the drug. There were no undesirable withdrawal symptoms noted.

Cortisone produced no constant effect on the Rh antibody titer, either to suppress or reduce the levels. The highest titer observed was 1:2,048 in a

patient with very severe diabetes who had lost one previous erythroblastotic baby. She received seven weeks' therapy and the pregnancy was terminated by cesarean section successfully at 37 weeks' gestation. She was again managed similarly and successfully one year later under the same regimen. In both pregnancies her insulin requirements were observed to increase as soon as cortisone was begun.

There was no known reactivation of pulmonary tuberculous lesions. Each

woman was carefully screened, however, prior to therapy.

There was no instance of activation of diabetes or increase of either bleeding or coagulation time often described among the untoward reactions to cortisone.

Likewise, no abnormal variation of any consequence was observed in either the hematocrit, hemoglobin, red or white blood cell counts or differential white cell count, with the exception of the expected suppression of eosinophils. The last was observed to drop gradually in all but 9 women. In 5 of these there was a moderate decrease and in 4 no change. Attempts to correlate the eosinophil response with fetal survival proved fruitless.

TABLE III. UNTOWARD REACTIONS TO CORTISONE

No reaction	20 women
Mild reactions	22 women
Moderate edema	11
Depression	3
Nervousness	3 2 2
Hirsutism	2
Edema, weight gain, hypertension Pigmentation increase Euphoria Painful nodules Mild glycosuria Insomnia Brawny neck edema Rash Garrulousness Vomiting	each 1
Acne Vertigo	
Severe reactions	3 women
Acne	1*
Nausea, headaches	1
Psychosis	ī

<sup>\*</sup>Infant also exhibited acne.

#### Effect of Cortisone on the Infant

With the exception of the one infant born with acne, no other untoward reaction attributable to cortisone was noted in the infants in this study. There were no gross fetal anomalies observed.

In one instance intrauterine fetal "tone" and activity were definitely observed to improve as soon as cortisone was begun. This has been reported.<sup>3</sup> No withdrawal symptoms were observed in the infants.

#### Results

A total of 45 pregnant white women were treated during the period of August, 1951, to August, 1954. All the husbands were Rh positive. From the past obstetrical histories 40 of them had delivered from one to 5 erythro-

blastotic infants (Table IV). Five women had not delivered affected babies previously but, due to the presence of alarmingly high antibody titers, were included, for comparison, in the early months of the study.

TABLE IV. RESULTS OF CORTISONE THERAPY RELATIVE TO NUMBER OF PREVIOUS ERYTHRO-BLASTOTIC INFANTS

	NUMBER OF PREVIOUS ERYTHROBLASTOTIC INFANTS	NUMBER OF WOMEN	LIVE BABY	NEO- NATAL DEATH	STILL- BIRTH	TOTAL FETAL LOSS	PER CENT MORTALITY*
_	One	22	17 (4 Rh-)	4	1	5	27.8
	Two	12	9 (1 Rh-)	1	2	3	27.3
	Three	2	0 .	0	2	2	100.
	Four	2	2	0	0	0	0
	Five	2	1	0	1	1	50.
	None	5	3	0	2†	2	40.
-	Total	45	32	5	8	13	

\*Excluding women who had Rh- negative infants.

†One complicated by abruptio placentae.

Excluding 5 Rh-negative infants from the evaluation of fetal survival, the mortality varied from 0.0 per cent (2 mothers who had delivered 4 erythroblastotic babies each previously) to 100 per cent (2 mothers who had delivered 3 affected infants each).

Although the comparative groups thus analyzed were small, there was no correlation between the past history and fetal survival. Forty per cent of the infants of women who had excellent previous histories were lost.

Twenty women had lost one and 5 had lost 2 infants previously (Table V). In this group there were 21 babies born alive. Seventeen survived, 5 of whom were Rh negative. Two babies that survived were born of a diabetic mother who exhibited an antibody titer of 1:2,048. One neonatal death occurred in an infant with a marked clinical picture of hydrops fetalis, a classical "Buddha" who lived for 51 hours. Two neonatal deaths are considered to have been preventable. In one instance an inexperienced resident physician attempted a transfusion. This baby, otherwise normal, died of sepsis. The other death occurred at the beginning of the study and because of the favorable clinical appearance of the infant, in spite of laboratory evidence to the contrary, transfusion was delayed. The fetal loss in this analysis was 40 per cent or if corrected 30 per cent. The findings seemed consistent with what one would expect of any mother with a similar obstetrical background.

TABLE V. RESULTS OF CORTISONE THERAPY IN WOMEN WHO LOST PREVIOUS INFANTS

	25	17	4	4	8 otal mortality	40
Two	5	2	2‡	1	3	60
One	20	15 (5 Rh nega- tive)*	2†	3	5	33,3
NUMBER DIED PREVIOUSLY	NUMBER OF MOTHERS	SURVIVING INFANTS	NEONATAL DEATHS	STILLBIRTH	FETAL LOSS	PER CENT MORTALITY

\*Of 10 Rh-positive infants, two were from diabetic mothers; one died at 15 months of kernicterus.

†One "Buddha" lived 51 hours.

‡Both considered preventable.

The duration of cortisone therapy extended from less than three weeks (2.1 Gm.) in 7 women to over twelve weeks (8.4 Grams) in 6 women, one receiving sixteen weeks' therapy (11.2 Gm.) (Table VI). Eliminating the Rh-

negative infants, the statistical result was not related to dosage but proved equivocal. Of the babies capable of being affected, the highest fetal loss was present both in the group that received less than three weeks of therapy and those who received it for twelve weeks or more. The duration of cortisone therapy with relative uniform dosage could not be used to predict the degree of fetal survival.

TABLE VI. DURATION OF CORTISONE THERAPY IN 45 WOMEN

DURATION OF THERAPY IN WEEKS	NUMBER	LIVE BABIES	DEAD BABIES (NEONATAL DEATHS)	STILLBIRTHS	FETAL LOSS	PER CENT MORTALITY
< 3	7	5	1	2	3	42.8
3 - 6	11†	10	2	1†	3	20.0
6 - 9	11	10 (2 Rh-)	2‡	1	3	33.3
9 - 12	10	8 (1 Rh-)	0	28	2	22.2
12 + (Longest 16)	6	4 (2 Rh-)	0	2	2	50
Total	45	37 (5 Rh-)	5	8	13	

\*Excluding Rh-negative infants.

†Therapy discontinued in one because of psychosis. Carried to term (stillbirth).

‡Both considered preventable deaths.

§Placental separation (abruptio) not related to Rh in one stillborn infant.

||Infant Rh negative.

Of 45 infants born, 37 were born alive and 8 were stillborn (Table VII). Five were Rh negative, 2 were mildly affected and were not transfused. Thus 32 infants exhibited varying degrees of erythroblastosis (71.1 per cent).

TABLE VII. FATE OF INFANTS

	NUMBER	PER CENT OF TOTAL
Total infants	45	
Born alive	37	82.2
Stillborn	8	17.7
Rh negative	5	11.1
Erythroblastotic infants	32	71.1
Exchange transfusion	23 (2 died)*	
Multiple transfusions	7 (3 died) †	
Erythroblastotic infants salvaged	27 (84.3%)	*

\*One "Buddha."

†Two deaths preventable.

Thirty of these received transfusions. Twenty-three were given exchange transfusions, two of whom died. One of these infants was the hydropic "Buddha."

Seven received multiple transfusions; there were 3 deaths, two of which were considered preventable as before mentioned. Twenty-seven of 32 Rhpositive, erythroblastotic infants in this group survived (84.3 per cent).

# Comment

It is difficult to derive any uniformity from the results in this study. We have conclusive evidence that cortisone may be administered to pregnant women up to 100 mg. daily, with a minimum of side effects, provided meticulous observations are made. There is likewise no evidence of any ill effect on the fetus. On the contrary, cortisone may mask the true clinical condition of the erythroblastotic baby, delay clinical jaundice, and, as a result,

produce a false sense of security. Although pregnandiol and/or 17-ketosteroid studies as described by Hunter<sup>3</sup> were not performed, these women received constant cortisone therapy. There was no correlation found between the number of previous affected babies or length of therapy and ultimate fetal survival.

The most disappointing finding was the inability of cortisone to *prevent* intrauterine fetal death and fetal hydrops. Both occurred regardless of the length of therapy.

We have been unable to confirm the belief that adequate cortisone levels in the last trimester of pregnancy in sensitized Rh-negative women will prevent hemolysis in the fetus and allow delivery of a healthy child.

Although the total number of women studied who delivered infants with effects of Rh sensitivity was only 39 (32 live erythroblastotic, 7 stillborn) this represents a sample of the pregnant population in the neighborhood of 15,000 pregnant women.

Cortisone therapy has not been shown to improve fetal survival significantly when compared to the use of exchange transfusion alone. These experiences are somewhat in agreement with those of Christensen and associates, whose conclusions parallel ours.

TABLE VIII, RESULTS OF CORTISONE THERAPY, INFANT MORTALITY

		DEATHS		PER CENT MORTALITY	
	TOTAL	TOTAL	PREVENTABLE	TOTAL	CORRECTED
Babies born	45	13	6	28.8	15.5
Live babies	37	5	2	13.5	8.1
Erythroblastotic	32	5	2	15.6	9.4
Stillborn	8*				

<sup>\*</sup>One stillbirth due to abruptio placentae.

The final summary of the results of treatment will be found in Table VIII. Of 45 women who received cortisone, 37 delivered liveborn babies; 32 of these infants were Rh positive and exhibited signs of erythroblastosis. There were 8 stillbirths, one of which was due to premature placental separation.

The total fetal deaths were 13 (28.8 per cent). If preventable deaths (2) and inadequate therapy (4 cases) are taken into consideration the corrected total fetal mortality was 15.5 per cent (7 infants).

The mortality of 32 liveborn babies was 15.6 per cent; if corrected (2 preventable deaths) it was 9.4 per cent. These findings do not compare with those in published reports<sup>3</sup> where the mortality for babies born alive was reduced from 10 per cent with transfusion alone to 3 per cent and stillbirths from 17 per cent to 5 per cent by administration of cortisone to the pregnant mother.

The variation in clinical findings must be due in part to the selection of patients. We feel that to prove of value, cortisone should have proved successful in those women who had histories of previously having delivered affected babies.

In this study cortisone has not improved the fetal survival in this group.

# Summary

- 1. Forty-five Rh-negative isoimmunized pregnant women, 40 of whom had previously produced babies affected by erythroblastosis, were studied and given cortisone in the last trimester of pregnancy in an attempt to improve fetal survival.
- 2. Under meticulous control and selection of patients, the drug was well tolerated by both mother and baby. There was one major reaction in a mother, none in any infant. All reactions were reversible.
- 3. There were 37 live babies, 8 stillbirths and 5 neonatal deaths. Five liveborn babies were Rh negative.
- 4. The over-all fetal mortality rate was 28.8 per cent, corrected to 15.5 per cent if 2 preventable deaths and 4 instances of inadequate therapy are deleted.
- 5. The women studied represent a pregnant population of approximately 15,000 pregnant women.
  - 6. Cortisone did not improve the fetal survival in the group studied.

#### Conclusion

The over-all infant survival correlated with past obstetrical history and duration of drug therapy has not shown sufficient improvement to justify continued use of cortisone in treatment or prevention of erythroblastosis fetalis.

The potent weapon in this problem still remains immediate exchange transfusion.

We are especially grateful to Misses Frances Street and Sue Bailey, serological technicians of Dr. Davenport, and to Misses Goldie Bartus and Joan Roddy, laboratory technicians in the Department of Obstetrics and Gynecology, whose combined efforts through these many months contributed the invaluable laboratory data to make this study possible.

The statistical data presented were analyzed by Dr. Hulda Bancroft, Biostatistician at Tulane University.

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#### Discussion

DR. EDWIN J. DECOSTA, Chicago, Ill.—During the past three years there have been a dozen references to the use of cortisone and/or ACTH in the management of pregnancy in the Rh-negative sensitized woman. These publications include one to a dozen odd case reports. Some of the authors enthusiastically endorsed cortisone as a

valuable agent in lowering the perinatal loss associated with erythroblastosis. Others failed to observe any real benefit. As always, the enthusiasts were heard; they are even quoted in the lay press. This contradiction makes critical evaluation particularly desirable because, if cortisone is without value, both the physician and his patient should be so apprised.

Much of the confusion in the literature arises, I believe, from a fact, which is often overlooked. A woman who has lost an erythroblastotic baby can still give birth to an erythroblastotic baby which may survive. Earlier this year, Drs. Gerbie, Potter, and I called attention to the observation that, without any special therapy, approximately 35 per cent of Rh-negative immunized mothers, who have suffered previous perinatal fetal loss, may deliver liveborn infants. If Rh-negative babies are deleted, this expectancy drops to 24 per cent. Immediate replacement transfusion should ensure at least a 90 per cent survival of liveborn erythroblastotic babies.

With respect to fetal loss, I would like to compare the experience of Dyer's treated patients who have previously lost an erythroblastotic child with the experience with a similar group of untreated controls which we reported. Note that in the 25 cortisone-treated patients there were 8 perinatal losses, whereas in our control series of 38 patients there were 22 perinatal losses. Eliminating the Rh-negative infants, these losses are 40 per cent and 71 per cent, respectively. The results certainly seem to favor cortisone. In spite of this, the use of cortisone in our experience was completely without benefit. It is difficult to understand why Dr. Dyer and his colleagues, on the basis of their excellent results, are not more enthusiastic about cortisone.

You will observe that in our control group a marked fetal loss was encountered prior to delivery: approximately 50 per cent of the Rh-positive babies were stillborn. In the present series this percentage is only 17.7. In that reported by Hunter using cortisone, it was 5 per cent. There is at least one possible answer to these variations. Perhaps we are not talking about the same thing. For example, if cortisone is begun during the last weeks of pregnancy, one automatically eliminates the stillbirths which have occurred earlier. Selection of cases makes a world of difference in the results.

I know of no treatment which will prevent the development of erythroblastosis when an Rh-positive child is carried by a sensitized mother. It should be remembered, however, that for reasons unknown the degree of damage may vary from one gestation to the next. In one pregnancy, death may occur in the twentieth week; in another it may not occur until delivery or after. This observation opens up another possible approach to therapy. We know that if these babies are alive at birth, we can save the great majority by replacement transfusion. We also know that the incidence of intrauterine death increases in proportion to the duration of gestation. Perhaps, therefore, we should try to deliver the baby early, but not too early, because prematurity itself is a serious hazard. Our aim is to deliver a fetus that is not irreparably damaged by circulating antibodies, yet is large and mature enough to survive. This type of delivery has been called preterm. Admittedly it is very difficult to determine the most propitious moment for such termination of pregnancy, but this is a method of management that seems worthy of serious consideration.

I take exception to one inference, namely, that cortisone does not affect the fetus. Although the authors may not have observed deleterious effects, we have. One patient, having been treated with less than 100 mg. of cortisone daily for severe eczema, delivered an edematous baby with a Cushing-like syndrome. Miraculously, the baby survived.

I want to reiterate that I agree with their conclusion—namely, that cortisone is without value in the treatment of erythroblastosis. In addition, and in a spirit of helpfulness, I want to present them with three more or less valuable reprints on this subject, 1-3 which apparently they have overlooked. It seems most desirable that a paper which carries so important a message should also have an all-inclusive bibliography.

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DR. DYER (Closing).—It is interesting to compare the control group with our series, as DeCosta did. You can imagine that in the little over three years that this study was in progress, there were occasions when perhaps five, six, or seven babies in a row would give us a response that made us very enthusiastic, particularly in the diabetic I mentioned. Certainly, if you have a woman who has delivered five erythroblastotic babies previously and who then has a baby survive, she will do everything short of naming the baby "Cortisone."

But then, as we went along, we had as many as five or six deaths in a row, making it a very pessimistic study. No doubt, the selection of patients is the answer. DeCosta mentioned that, and I am sure that if you will look at the articles (not the ones that I have been so fortunate as to receive, but the articles I mentioned in my bibliography) you will find such statements as, "We treat women in whom—according to the findings of antibodies in their blood—there is a poor prognosis predicted for the child." Well, if we went along with that line of thinking, I am certain you would find most of the mortality rates decreased, and fetal survival rates increased.

In mentioning the effect on the fetus, I did not mean to convey the impression that cortisone is a drug that will not affect a baby. I merely made mention of the fact that in this series of the babies born alive (37 of them born alive), there was no known effect of cortisone seen in the babies, and each of these babies was seen by our pediatrics pathologist and consultant.

Whether or not delivery of these infants prematurely will increase fetal survival, I do not know. We have not had particularly good results in using that method routinely.

# EXPLORATION OF THE UTERUS FOLLOWING DELIVERY\*

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E XPLORATION of the uterus following delivery is not a new procedure. It has been considered good obstetric practice to explore the uterus after version, craniotomy, decapitation, manual removal of the placenta, in all cases of postpartum hemorrhage, or any suspected case of ruptured uterus. The routine exploration of the uterus is not an accepted procedure.

Death from pulmonary embolus and prolonged morbidity from pelvic and femoral thrombophlebitis have almost disappeared from our obstetric morbidity lists since the advent of early ambulation, antibiotics, and the blood bank. The success of early ambulation eventually led to early discharge from the hospital. The well-being of the ambulant parturient, her anxiety about other children at home, and the demands placed upon the obstetrical facilities of the hospital were all responsible for this practice. In our institution patients were discharged on the fourth or fifth postpartum day. This limited observation of the patient carried with it certain dangers not considered previously. It was noted with some concern that a small percentage of these patients returned to the hospital because of uterine hemorrhage. These women were being admitted with various degrees of blood loss and shock. In every instance the cause was retained placental tissue. Review of the records in every case revealed that the placenta was examined and declared to be intact. In attempting to find a solution to this problem we considered the use of routine exploration of the uterus. It appealed to us as a more certain method of discovering the missing placental tissue. Three big questions had to be answered: Would it increase morbidity rather than reduce it? Was it a safe procedure? Would it answer our problem?

#### Material Studied

We began to examine our private patients following delivery in 1946. In the beginning we changed the patient's drapes and our gowns and gloves. This procedure was altered during the years, 1946-1948. Records were kept and in 1949 we felt we were well enough versed with the procedure and had such an established technique that statistics could be presented. During the next four years the uterus of every patient delivered by myself or my associate, Dr. Thomas M. Tierney, was explored by the attendent and the resident. This period of time provides the first half of this thesis. To have a rebuttal to the argument, "What would occur to your statistics if everyone did it?" we asked the open staff of the hospital to explore all uteri beginning Jan. 1, 1953. From this group we divided our cases into those who had been delivered by Board or Board-eligible men, by men in the general practice of medicine, and those cases in which the uterus was not explored, which we used as a control. These three groups were then compared to those in the original study.

<sup>\*</sup>Presented at the Twenty-second Annual Meeting of the Central Association of Obstetricians and Gynecologists, St. Louis, Mo., Oct. 7 to 9, 1954.

# Technique

At the time of delivery the patient was placed in the lithotomy position. The perineal area was cleansed with Septisol solution and rinsed with sterile water. The hand basins contained only sterile water. The patient was draped and the delivery was accomplished. Ergotrate, 3 minims, was given intravenously with the delivery of the shoulders. Following delivery of the placenta and prior to episiorrhaphy the vulvar area was again cleansed with sterile water from the hand basin. The gloved hands were rinsed in the hand basins, and the uterus was explored in the following manner: The cupped hand was introduced into the uterus, and the anterior wall, the fundus, and the posterior wall were each in turn evaluated. The size of the uterine cavity, its shape, any irregularity, placental tissue, membranes, anomalies, tumors, and the placental site were all noted. The findings were dictated to the supervisor at the time of exploration on a chart provided for that purpose. The postpartum care of the patient was routine. Antibiotics were not used unless morbidity occurred. Gloves were not changed during the delivery unless grossly contaminated.

# Results

The purpose of this paper is to show our experiences with routine exploration and to establish, if possible, that this procedure reduces the number of patients who return to the hospital because of delayed hemorrhage, what its effects upon morbidity are, and whether it is safe for all physicians to use.

During the years 1945 to 1954, the number of deliveries in this institution has almost doubled, yet the hospital physical capacity has not. Following World War II there was an increase in the number of deliveries which has not diminished.

From Jan. 1, 1949, to Dec. 31, 1952, 1,269 private patients were delivered by myself or my associate (T. M. T.) (Table I). Thirty-four of these were delivered by cesarean section (2.75 per cent) and 1,235 were delivered through the birth canal. This table shows a conservative attitude in the handling of these patients. Of this group 1,127 patients were delivered spontaneously or by outlet forceps.

TABLE I. TYPES OF DELIVERY, FIRST GROUP, 1949-1952

Spontaneous		861
Low forceps		266
Midforceps	•	56
Breech		47
Version and extraction		5
Total vaginal deliveries		1,235
Cesarean sections		34
Total deliveries		1,269

The findings in the exploration of 1,235 uteri are presented in Table II. There were no pathologic findings in 1,135 patients. Eighteen patients had retained placental tissue and 74 patients had retained membranes. It is an accepted principle that not all patients who have retained tissue have difficulty. Some of these patients might expell the retained placenta without severe clinical complications. There is no way to determine which will and which will not have trouble. Retained membranes seldom cause any difficulty. They are usually expelled or slough away as a catabolic process. Eight of the patients presented unsuspected pathology. Three had an incomplete septum in the upper portion of the uterus. All 3 delivered without difficulty but all had breech presentations. One of these patients delivered again in 1954 and again had a breech presentation. Is this just a coincidence?

TABLE II. INTRAUTERINE PATHOLOGY, FIRST GROUP

Placental tissue	18
Membranes	74
Incomplete uterine septum	3
Bicornuate uterus	2
Submucous fibroid	3
No pathologic findings	1,135

Submucous fibroid was found in 3 patients. All of these were about the size of a plum and one was pedunculated. Two patients were found to have bicornuate uteri.

The standard of morbidity set by the American College of Surgeons of 100.4° F. on two successive days after the first 24 hours seems to be too lenient. D'Esopo introduced a morbidity index in 1950 and Hesseltine offered a modification of it in 1953. Whether these new approaches to this problem will be accepted remains to be seen.

In Table III, we show the number of patients who had fever but not sufficiently high to be included under the American College of Surgeons standard. Ninety-three patients ran a temperature of 99° F. or over and are included in this group. Over half of this group had fever in the first 24 hours.

TABLE III. NONMORBID TEMPERATURE, FIRST GROUP

First day	56
Second day Third day	20
Third day	9
Fourth day	8
Total	93

There were 32 morbid patients. This group will be analyzed to determine if factors other than the uterine explorations might have some bearing on the morbidity. Parity and the type of delivery are reviewed in Table IV. Twenty-one of the 32 patients were primigravidas and 16 of these had simple deliveries. Seven of the multiparas also had simple deliveries. The uncorrected morbidity in this group was 2.5 per cent.

TABLE IV. MORBIDITY, IN RELATION TO METHOD OF DELIVERY, 32 PATIENTS, FIRST GROUP

METHOD OF DELIVERY	PRIMIPARAS	MULTIPARAS
Spontaneous	11	6
Low forceps	7	2
Midforceps	2	3
Breech extraction	1	0
Total Morbidity 2.59%	21	11

TABLE V. MORBIDITY CAUSES, FIRST GROUP

Genital.—			
Infected episiotomy	1		
Hematoma of vulva	1		
Endometritis	22		,
Total	_	24	
Extragenital.—			
Urinary tract infection	6		
Urinary tract infection Perirectal abscess	1		
Postpartum psychosis	1		
Total	_	8	

Continuing the analysis of the 32 cases of morbidity (Table V), 24 were considered to be of genital focus and 8 extragenital. The vast majority of the genital group were diagnosed as endometritis; there was one infected episiotomy and one hematoma of the vulva.

Urinary tract infection accounted for 6 of the 8 extragenital cases. A large perirectal abscess present antepartum is included in this group and one patient who developed a postpartum psychosis.

In the group classified as having endometritis (Table VI) we feel that the difficulty encountered in delivery was sufficient to account for some of the morbidity. These include 5 deliveries by midforceps, one manual removal of the placenta, and 2 cases of placenta previa with delivery through the birth canal. Blood transfusion reaction in these 2 cases might have been the cause of the morbidity but we chose to classify them as endometritis.

TABLE VI. MORBIDITY IN FIRST GROUP DUE TO ENDOMETRITIS

Endometritis	22 cases
Delivery Factor.—	
Midforceps	5
Breech extraction	1
Manual removal of placenta	1
Placenta previa	2

\*Blood transfusion reaction may have been the cause of two cases which were considered as endometritis.

The next phase of the presentation was to compare the results of this group with the results of the other groups. In Table VII, we show the type of delivery in the four groups. Group A constitutes the original group of 1,235 patients presented in the first half of this paper. Group B is a group of 916 patients delivered during 1953 by Diplomates of the American Board of Obstetrics and Gynecology or by men who by training and experience were eligible to take the examination for certification by the Board. The uterus in all of these patients was explored following delivery. Group C is a group of 1,104 patients delivered exclusively by general practitioners during 1953. In all of these patients the uterus was explored. Group D is a group of 1,098 patients delivered in 1953 who did not have the uterus explored. It is worth noting that the numbers in each group are not far apart. The conservative tendency of the department is again shown in this table. In the 4,353 deliveries shown, 2,933 were spontaneous, and 1,057 by outlet forceps. This is approximately 4,000 of the 4,353 deliveries.

TABLE VII. TYPES OF DELIVERY, ALL GROUPS

	GROUP*				
	Λ	В	C	D	
Spontaneous	861	516	788	768	
Low forceps	266	268	283	240	
Midforceps	56	64	10	18	
Breech	47	60	15	28	
Version and extraction	5	. 8	8	4	
Total	1,235	916	1,104	1,058	

\*Group A, Original Study.

Group B, Board or Board eligible.

Group C, General practice group.

Group D, Not explored (control).

The intrauterine findings are shown in Table VIII. In the general practice group the incidence of placental tissue and membranes is increased. Does this

1098

represent improper handling of the third stage of labor? Does it represent too hasty delivery of the placenta? Many of the patients in the general practice group were examined by the resident physician.

TABLE VIII. INTRAUTERINE PATHOLOGY, ALL GROUPS

	GROUP		
	A	В	C
Placental tissue	18	13	24
Membrane	74	70	90
Incomplete septum	3	2	1
Bicornuate uterus	2	1	0
Submucous fibroid	3	5	4

Table IX shows the number of patients in each group who had fever at any time during their stay in the hospital. The figures in this group remain fairly constant.

TABLE IX. NONMORBID TEMPERATURE, ALL GROUPS

	GROUP			
	A	В	C	D
First day	56	50	56	58
Second day	20	31	16	32
Third day	9	9	12	11
Fourth day	8	14	7	8
Total	93	104	91	109

The focus of the morbidity in each group is demonstrated in Table X. The percentage of extragenital cause of morbidity is fairly constant. It is interesting to note that Group B which is the group delivered by Board diplomates or Board-eligible physicians had the greatest morbidity (3.16 per cent) and Group C, those delivered by the general practitioners had the lowest (1.81 per cent). The Board of Health of the City of Chicago requires that all complicated deliveries other than those by outlet forceps have consultation unless the attending physician is a member of the senior obstetric staff of the hospital. All men in general practice are required to abide by this. When a consultant saw a patient in the general practice group and handled the delivery it was then included in Group B. Thus the major pathology of Group C was inherited by Group B. As a result of this, Group B had 64 midforceps deliveries and Group C, 10. Group B had 60 breech deliveries and Group C, 10. The average morbidity for the two groups would be 2.48 per cent. Group D, the control group, had a morbidity of 2.08 per cent. This is lower than either A or B in which explorations were performed. Again there is a decided difference in Group D in the more serious operative procedures.

TABLE X. MORBIDITY (FOCUS), ALL GROUPS

	GENITAL	PER CENT	EXTRAGENITAL
Group A	24	2.65	8
Group B	29	3.16	6
Group A Group B Group C	20	1.81	9
Group D	23	2.09	9

The type of delivery and the parity of the patients are presented in Table XI. In the entire group of primiparous patients, 83 in number, 14 had either midforceps or breech deliveries and in the multiparous group numbering 45, 12 had either midforceps or breech deliveries. Of 128 patients listed as morbid,

26 had midforceps or breech deliveries, which represent 20 per cent of the morbidity. Yet the group of midforceps and breeches represented only 6.8 per cent of the entire group. It appears that the type of delivery is a determining factor in morbidity.

TABLE XI. MORBIDITY IN RELATION TO METHOD OF DELIVERY

	GROUP			
METHOD OF DELIVERY	A	В	C	D
Primiparas				7.11
Spontaneous	11	10	16	14
Low forceps	7	5	2	4
Midforceps	2	5	1	0
Breech extraction	1	3	1	1
Total	21	23	20	19
Multiparas.—		-		
Spontaneous	6	2	6	7
Low forceps	2	6	1	3
Midforceps	3	2	1	2
Midforceps Breech extraction	0	2	1	1
Total	11	12	9	13

Table XII divides the morbidity into genital and extragenital causes. Endometritis, a rather loose classification, was the greatest single cause of morbidity. The extragenital causes of morbidity are included to demonstrate that unless it could be proved to have an extragenital cause, the morbidity was classed as genital.

TABLE XII. MORBIDITY CAUSES, ALL GROUPS

	GROUP				
	A	В	C	D	
Genital Causes.—					
Infected episiotomy	1	1	0	1	
Infected episiotomy Hematoma of vulva	1	0	0	0	
Endometritis	22	28	20	22	
Total	24	29	20	23	
Extragenital Causes.—					
Urinary tract infection	6	6	7	. 6	
Postpartum psychosis	1	0	0	1	
Perirectal abscess	1	0	- 0	0	- 2
Aspiration pneumonia	0	0	1	0	*
Mumps	0	0	0	1	
Upper respiratory infections	0	0	1	1	
Total	8	6	. 9	9	

In Table XI we discussed the delivery factors as an influence on morbidity. Table XIII seems further to confirm this opinion. In 34 of the 82 cases listed as endometritis there was a delivery factor which could account for the morbidity. This delivery factor of 41.5 per cent seems to demonstrate conclusively that the type of delivery affects morbidity more than any other single factor.

In Table XIV we showed the number of explorations of the uterus in each group to determine if the number of explorations had any influence on the morbidity percentage. It appears that it had little influence.

Some patients returned to the hospital for bleeding. In Groups A, B, and C, which were the groups that had uterine exploration, only one patient returned and this patient had no placental tissue and required hysterectomy to control the bleeding. In Group D, 6 patients returned. All patients who returned to the hospital required curettages and blood transfusion and all had retained placental tissue.

TABLE XIII. MORBIDITY, ALL GROUPS, DUE TO ENDOMETRITIS

	GROUP			
	Λ	В	C	D
Endometritis	22	28	20	22
Delivery Factor.—				
Low forceps	0	1	3*	3*
Midforceps	5	7	0	0
Breech extraction	1	3	1	1 :-
Placenta previa	2	2	0	0
Prolonged labor	0	2	1	1
Uterine pack	0	0	0	1
Total	8	15	5	6

<sup>\*</sup>Pelvic trauma.

TABLE XIV. SUMMARY OF MORBIDITY

		GROUP		
	A	В	C	
No. deliveries	1,235	916	1,104	
Morbidity per cent	2.65	3.16	1.81	
No. explorations	2,634	1,592	1,216	

## Comment

In a group of 3,255 patients who had uterine exploration only one returned to the hospital for bleeding. While in the control group of 1,098 cases 6 returned for bleeding from retained placental tissue. We feel that this answers our original premise as to whether or not uterine exploration would prevent patients from returning to the hospital. We know it will. It appears to be a safe procedure for everyone to use but we must qualify this by stating that it cannot be accepted as such until studies by other groups either substantiate our claim or prove it wrong. It is also our opinion that morbidity was not increased appreciably by the procedure and that the latent morbidity was lowered. Hoffman's recent paper on "Routine Manual Removal of the Placenta" corroborates this opinion.

Uterine exploration gives more information that has been brought out in this paper. The site of the placenta is easily determined and with the examining hand within the cavity of the uterus the outer surface of the uterus can easily be examined by the free hand, as well as the adnexa. All who have come to use this procedure have added it as a part of their delivery technique. We offer it for your considered judgment.

# Summary

Routine exploration of the uterus: (1) reduced the number of patients who returned to the hospital for bleeding from retained placenta; (2) afforded better pelvic evaluation; (3) did not appreciably increase morbidity; (4) appears safe for all physicians to use.

Further evaluation of this procedure should be undertaken by other groups before definite conclusions are drawn.

## References

- 1. D'Esopo, D. Anthony: Am. J. OBST. & GYNEC. 59: 77, 1950.
- 2. D'Esopo, D. Anthony: Am. J. OBST. & GYNEC. 59: 104, 1950.
- Hesseltine, H. Close, and Bustamante, J.: Am. J OBST. & GYNEC. 68: 623, 1954.
   Hoffman, Ralph L.: Am. J. OBST. & GYNEC. 68: 645, 1954.

## Discussion

DR MORTON R. LAZAR, Detroit, Mich.—Dr. Hawkins' paper establishes the fact that the exploration of the uterus is a safe procedure. This is shown by the lack of morbidity and mortality in his series where each uterus was explored. The question arises, however, whether this procedure is necessary. The indications that we follow without hesitancy are that, if there is any question of completeness following expulsion of the placenta and membranes, or if the uterus does not contract well, an exploration of the uterus is done. The advantage of routinely exploring each uterus is, without argument, the finding of the occasional anomaly of the uterus or retained tissue which is missed, even though eareful examination of the placenta is done.

It is agreed that routine exploration of the uterus will prevent or decrease immediate postpartum hemorrhage. It is also agreed that the occasional delayed postpartum hemorrhage, which is caused by retained secundines, will be decreased. It is difficult for me to understand, however, how the majority of the cases of delayed postpartum hemorrhage can be prevented by this procedure. The majority of cases in which the patients return to the hospital in the late puerperium because of bleeding are not especially caused by retained placental tissue. Dieckmann substantiates this in his report in which he found that curettage rarely revealed placental tissue. Our experience is essentially the same.

The most common cause of delayed postpartum bleeding is a persistent or subinvoluted placental site. The clinical picture is the same as that of retained tissue. Williams described the exfoliative mechanism whereby the uterine mucosa regenerates after delivery. This is reported in his treatise written just before his death in 1931. The reason for the failure of proper vascular obliteration is not known. When this area is curetted, it is not uncommon to obtain much white, thick, hyalinized material with no retained placental tissue. It is difficult for me to comprehend, and I am sure that Dr. Hawkins will be glad to explain, if he does not agree, how routine exploration of the uterus can prevent this type of bleeding. This type of bleeding that occurs in the late puerperium constitutes one of the grave complications that the obstetrician encounters.

It is this type of bleeding that Melody calls the most treacherous. To have only one case out of 3,255 return to the hospital for curettage is a superlative record and Dr. Hawkins is to be congratulated.

DR. JOHN G. FLEMING, Cincinnati, Ohio.—Six years ago I had under my care a 32-year-old primipara who, with known fibroids in the uterus, delivered normally after a short labor. The placenta separated spontaneously, and appeared intact upon inspection. On the tenth day post partum, when at home in her kitchen, she suddenly began to hemorrhage, and was in deep shock upon arrival at the hospital. Removal of a large placental polyp, hidden behind a submucous fibroid in one cornu, only increased the hemorrhage, and hysterectomy was necessary to save her life.

Since then I have gradually widened my indications for exploration of the uterus following delivery, regardless of the stage of gestation, or the apparently intact condition of the secundines or placenta. The following advantages have been gained:

- 1. One knows that the uterus is empty, and any ensuing uterine bleeding may be treated appropriately with complete assurance that this is so.
- 2. Approximately one out of twenty-five deliveries will yield a fragment of placenta or membrane, which would eventually result in some degree of hemorrhage, possible rehospitalization, curettage, and economic loss of time and money for the patient.

- 3. Unsuspected intra- and extrauterine conditions, including variations in conformation of the uterine fundus, fibroids, and adnexal masses become known facts for both immediate and future management.
- 4. The introduction of the hand within the uterus seems to make it contract more rapidly, and to lessen postpartum hemorrhage.

One would expect complications to develop as a result of almost routine exploration. On the contrary, my experience has been that the procedure has not increased the incidence of puerperal morbidity, parametritis, laceration of the cervix, or phlebitis.

DR. HAWKINS (Closing).—Since the advent of antibiotics and blood banks, gynecological surgery has expanded greatly. Obstetrical expansion has remained dormant, and I believe there is a time and a place when this dormant state should give way to a little bit of flexibility.

# Original Communications

# GROWTH, PREGNANCY, AND CARBOHYDRATE METABOLISM\*

ARTHUR ST. GEORGE HUGGETT, M.B., B.S., Ph.D., D.Sc., London, England

(From the Department of Physiology, St. Mary's Hospital Medical School,

University of London)

THIS lecture was instituted by Dr. Joseph Bolivar DeLee as a memorial to his brother, Solomon Theron DeLee. Solomon Theron DeLee had helped his brother Joseph in his time of difficulty, had supported him financially, materially, and spiritually in furthering the work of Joseph in the relief of suffering in the labors of childbirth.

Though instituted by Joseph to mark his appreciation of and gratitude for aid without which he could not have accomplished his own work, the first lecture was not given till after his own death and by a process of mutation the lecture has come to be a memorial to both Solomon and the founder, his brother Joseph.

Joseph Bolivar DeLee was known to me by name and reputation from my student days as a great teacher and obstetrician. Still more he was known to those whose privilege it was to have been his students, his nurses, his colleagues, his friends and, most of all, his patients as an indefatigable altruist, idealist, and worker. His work was his life and his life was selflessly given to his patients and the art of obstetrics. It needs only a short visit to Chicago, to its Lying-in Hospital, to see its wards, theaters, and laboratories, and to meet his students, friends, and colleagues to realize that the personality of DeLee lives on in Chicago in this hospital and city.

Toxemia of pregnancy in women is characterized by hypertension and albuminuria with a variable incidence of nervous symptoms. In animals similar diseases occur with some of these symptoms. In sheep the nervous symptoms are accompanied by a well-marked ketosis. The liability to the disease is increased by the presence of twins or triplets (twin-lamb disease) or by a dietary shortage, whether due to poor pasture or to grass covered by snow falls. It can be produced experimentally by calorie shortage followed by a sudden fast especially in late pregnancy. The liver, post mortem, shows a deficiency of glycogen, fatty infiltration, but no necrosis. Prevention can be effected by restricting the protein (legumes) and ensuring an excess of calorierich foods (grass and pasture). Glucose administration will relieve the condition,

<sup>\*</sup>The Solomon Theron DeLee Lecture, given at the Chicago Lying-in Hospital of the University of Chicago, Oct. 26, 1953.

In the mare the predominant clinical picture is an eclampsia-like state, whereas in the cow there is more than one type of pregnancy disease as in the sheep. Cows showing a high proportion of butter fat are likely to get a ketosis. In both the mare and the cow as in the sheep the condition is relieved by intravenous glucose. It is permissible here to call attention to certain peculiar conditions of fetal growth in different species which bear upon problems of carbohydrates in the fetus and pregnancy.

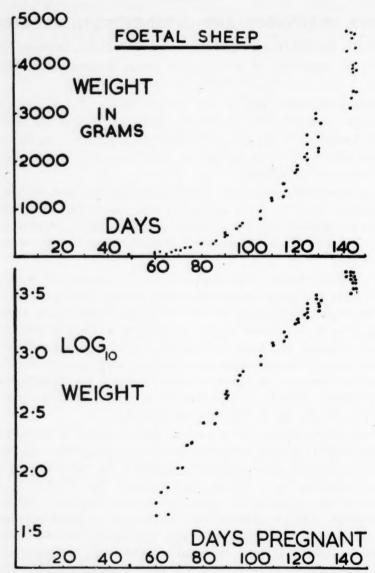


Fig. 1.—Upper half (Fig. 1,A) relates fetal age to fetal weight in sheep. Lower half (Fig. 1,B) relates the logarithm of weight (base 10) to the fetal age.

# Comparative Rates of Fetal Growth

There have been many attempts to express the rate of intrauterine growth mathematically. The attempts are reviewed by Needham (1931).

FOETAL SHEEP

0.45 (t-34)

# Number 5

20

10



40 50 60 70 80 90 100 110 120 130 140 150 DAYS PREGNANT

Fig. 2.—Length of sheep fetus plotted against age. (From Huggett and Widdas: J. Physiol. 114: 306, 1951, Cambridge University Press.)

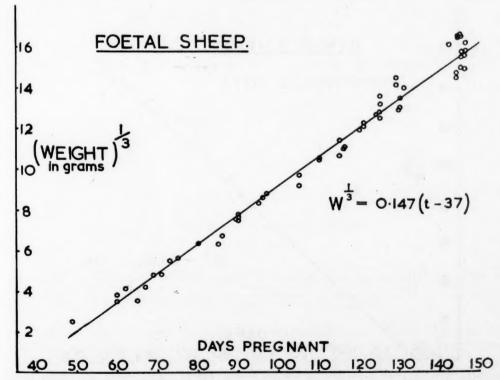


Fig. 3.—Cube root of weight of sheep fetus plotted against fetal age. (From Huggett and Widdas: J. Physiol 114: 306, 1951, Cambridge University Press.)

None have been satisfactory. Fig. 1 shows the curve of fetal weight plotted against conception age and also an attempt to express it logarithmically. It does not get one biologically any further than the original curve.

does not get one biologically any further than the original curve.

In 1951, my colleague, Dr. Wilfrid Widdas, endeavored to date the ages of sheep fetuses of unknown conceptual age (Huggett and Widdas 1951). Comparison of the curves of length/age and weight/age showed pronounced differences (Figs. 1, B and 2).

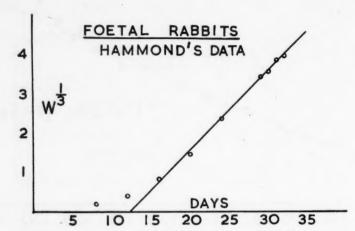


Fig. 4.—Cube root of weight of rabbit fetus plotted against fetal age. Data from Hammond (1914). (From Huggett and Widdas: J. Physiol. 114: 306, 1951, Cambridge University Press.)

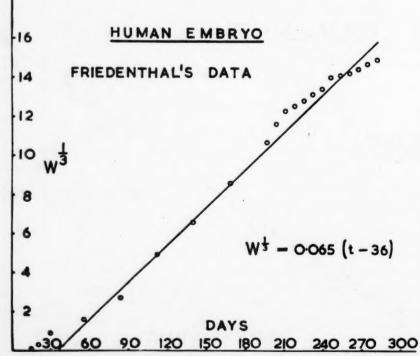


Fig. 5.—Cube root of weight of human fetuses plotted against fetal age. Data from Friedenthal (1914). (From Huggett and Widdas: J. Physiol. 114: 306, 1951, Cambridge University Press.)

Widdas postulated that, the density of an organism being fairly constant, then the ratio  $\frac{W}{V} = \frac{W}{L^3} = \text{constant}$ . This being so then the graph  $W^{1/3}/\text{Age}$  should be a straight line as in the graph L/Age. This was found to be the case (Fig. 3).

One reason why earlier workers had got unsatisfactory mathematical representation of growth in the uterus was because they had endeavored to find a single line fitting all points and passing also through the origin at the moment of conception. The new point about Widdas' concept was that the straight line did not pass through the origin. There are two lines, one for the second part of pregnancy and one for the first part. Data are available only for the second portion, the ages of the first line being histological and data unavailable.

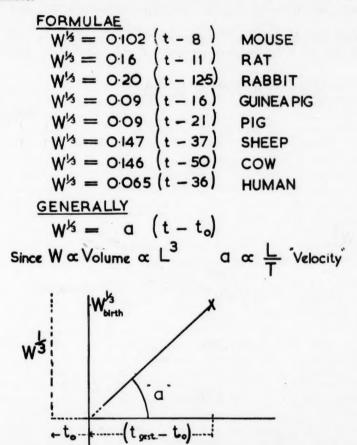


Fig. 6.—Graph of the generalized equation of growth in utero,  $W^{1/3}=a$   $(t_g-t_o)$ ,  $t_g$  being age at full term (gestation period),  $t_o$  being the fetal age at which the graph cuts the abscissa on prolongation back and a the angle made by the graph with the abscissa. In the upper half are particular values of the equations for different species. (From Huggett and Widdas: J. Physiol. 114: 306, 1951, Cambridge University Press.)

When the late line W<sup>1/3</sup>/Age is prolonged back it cuts the base line. Earlier than this it is following a different and slower course from conception (Figs. 4 and 5).

It is possible to generalize and to devise an equation for this straight line fitting the curve shown in Fig. 6.

$$W^{1/3} = a(t_g - t_o)$$
 $\therefore a = \frac{W^{1/3}}{t_g - t_o}$ 
 $a = \frac{W^{1/3}}{T} = \frac{L}{T}$ 

that is

where T represents a factor for time t<sub>g</sub> the age at full term

the age at which the line cuts the abscissa

 $\therefore$  a = a velocity or rate of growth and the bigger the angle a in Fig. 6 the greater the rate of growth in utero

Now when we examine where the straight line cuts the abscissa at to in different species we find that within a variation of ±15 per cent to is 40 per cent of tg in all species with gestation periods up to 50 days, 30 per cent between 50 and 100 days, 20 per cent between 100 and 400 days, and appears to be 10 per cent in gestation periods exceeding 400 days but data for this are inadequate.

Accepting this generalization, therefore, if we know tg and the normal birth weight at full term for any species we can calculate to for that species.

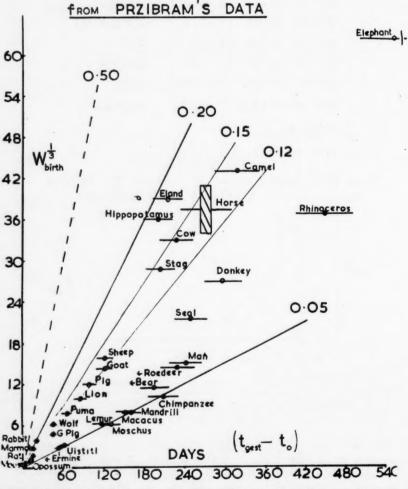


Fig. 7.—Przibram's (1927) data for the different mammalian species: the cube root plotted and the graphs relating  $t_o$  for different values of "a" drawn. (From Huggett and Widdas: J. Physiol. 114: 306, 1951, Cambridge University Press.)

Przibram (1927) has published gestation periods and birth weights of a large number of mammalian species. Let us calculate  $t_o$  for each species on the basis given previously and plot all the values for  $t_o$  at a common origin regardless of the difference between conception and  $t_o$ . Then let us plot the cube root of the birth weight for each species at the respective  $t_g$ . We thus have a pair of points for each species joined by a straight line. If we do then we obtain Fig. 7.

It is to be noted that a represents velocity of change of W<sup>1/3</sup>. Consequently, the actual growth rates of the fetuses are the cube of the relative values of a.

Fig. 7 shows us several things. First, no primate has a value for a exceeding 0.071 and all fluctuate around an average value of 0.05. For all non-primates other than whales the average value for a lies between 0.10 and 0.20 with a mean about 0.12. For whales the value a is 0.50. The actual growth rates of the fetuses are proportionate to the cube of the ratio of these values. That is to say, all primates grow at much the same rate and slower than other mammals. To achieve bigger fetuses at full term they have longer gestation periods.

All nonprimates other than whales grow at about 13 times the rate of the primates and the whales grow about 1,000 times as fast in the uterus as a human being. Since the gestation period of the sperm whale is eleven months and its fetus weighs 3 to 4 tons, this is comprehensible and forms an interesting comparison with the human 7 pounds after nine months in the uterus.

When, therefore, we look at intrauterine growth on a comparative basis we find very great contrasts between different species from the slow-growing primate to the faster nonprimate and the lightning flash of the whale. Rates of water, mineral, and nitrogen retention and deposition must vary and mitotic indices and energy consumptions must be on a scale according to the three groups studied.

## Growth Rate and Umbilical Blood Flow

Grosser's (1927) classification of placentas has served a useful purpose as a working hypothesis for orderly thought upon the relations between transmission of foodstuffs and placental structure. The basic fallacy was the implication that materials passed more or less by diffusion, that the less the distance between the two blood streams the greater the ease of passage of the material in question. The subsidiary implication is that the hemochorial is a "higher" type of placenta than an endotheliochorial or a syndesmochorial and, including Mossman's (1937) hemoendothelial type in rabbits, that this latter is "higher" still than the hemochorial type of human beings. Dempsey and Wislocki and their colleagues have shown that the activity of the placenta measured histochemically does not depend upon the thickness or number of layers between the blood streams nor upon the size and shape of cells, but upon the enzymes present, especially the phosphatases.

Two aspects of this can be estimated quantitatively, the distance between the streams of blood and the rates at which blood flows. This was later attempted by Barcroft and Torrens in 1946. A very beautiful estimate was made by Greenfield in 1948. He enclosed the fetus in a box which being sealed by an air seal acted as a plethysmograph (Cooper and Greenfield 1948). The rate of decrease of fetal volume on occlusion of the umbilical cord with an air pressure intermediate between the arterial and venous blood pressures was a measure of arterial flow in the umbilical artery (Cooper, Greenfield, and Huggett

1948).

The experiments were conducted upon animals, sheep and guinea pigs, and also in the human subject. The sheep were anesthetized spinally, cesarean section performed, and the mother, uterus, and fetus immersed in a bath of saline at 38° C. (Fig. 8). The principles involved in the plethysmograph are illustrated in Fig. 9 and the type of tracing obtained is shown in Fig. 10, both taken from a paper by Greenfield, Shepherd, and Whelan (1951) in which they recorded the blood flow in a human fetus during a therapeutic abortion at the fourth month.



Fig. 8.-Sheep bath.

Measured in this way the average blood flow in the sheep was 130 ml. per minute, in the guinea pig 2.5 ml. per minute, and in the human being at the ninety-third day of fetal life it was 2.1 ml. per minute. When these rates of blood flow are conjoined to the rates of growth in fetuses of different species as ascertained by Huggett and Widdas (1951), it then transpires that to deposit at any fetal age 1 gram of fetal tissue the sheep needs 5.5 L. of blood per minute, the guinea pig 1.28, and man 1.07 L. (Fig. 11). Reynolds, Light, Ardran, and Prichard (1952) have shown that the figures previously quoted and obtained by my colleagues in the British Isles are probably on the low side. With Dr. F. W. Light of Johns Hopkins and Dr. Marjorie Prichard and Dr. Ardran of the Nuffield Institute at Oxford, Reynolds has perfected a beautiful cinematographic technique for measuring blood flow. Nevertheless, the species differences found by Greenfield still stand.

## Fetal Carbohydrates—Glycogen

In the adult body carbohydrates are found in four main sites: in the blood as sugar, in the muscles as glycogen, in the liver as glycogen, and in the nervous system as galactose. In lactating women they are secreted as lactose. In the developing ovum carbohydrates are present both in the fetus and in the placenta. In the fetus they appear in the liver and muscles mainly as glycogen and in the blood as glucose, and in the placentas of many mammals

as glycogen, quite apart from the composition of Wharton's jelly. In addition there is ribose in all nuclei which implies greater ribose metabolism in the dividing nuclei of growing tissue. Finally, certain mammals have in addition to glucose considerable quantities of fructose in their fetal blood. The two forms of carbohydrates upon which it is proposed to concentrate in this lecture are glycogen of the placenta and fructose of the fetal blood.

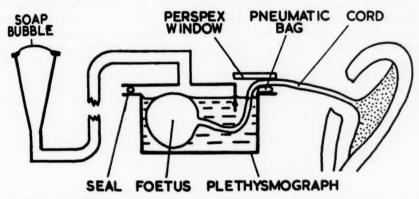


Fig. 9.—The fetal plethysmograph. (From Greenfield, Shepherd, and Whelan: Lancet 2: 422, 1951.)

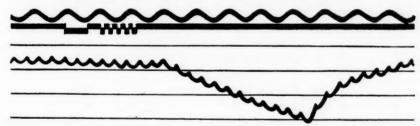


Fig. 10.—A typical record of the volume of the human fetus enclosed in a plethysmograph while the umbilical vein was occluded. The top tracing represents the time in seconds; the middle tracing the identifying signal; and the lower tracing the fetal volume curve, showing changes during and after inflation of the bag to 22 mm. Hg. The horizontal lines represent changes in volume of 0.05 ml. The flow was 1.6 ml. per minute. (From Greenfield, Shepherd, and Whelan: Lancet 2: 422, 1951.)

In 1855 Claude Bernard found that the blood of the fetal calf contained fructose and that it was also present in the amniotic and allantoic fluids. There was no further work on this until 1907 when Paton, Watson, and Kerr found it in sheep in the fetal blood and also in the amniotic and allantoic fluids. In 1922 Orr found it in human and Takata in whale fetal blood. The identification by Bernard rested on the levorotation and by Orr and Takata upon the qualitative color reaction with resorcinol, the Selivanoff test.

In 1859 Claude Bernard showed that the placenta of the rabbit contains glycogen which he also found in the liver. Chipman, working first in Edinburgh (1903) and later in Montreal at the Royal Victoria Hospital, demonstrated that histologically the glycogen was in the decidua. Lochhead and Cramer in 1908 followed up Chipman's work with a chemical determination and also showed its constancy under experimental conditions. Meanwhile in 1907 Driessen had published in Germany a description of glycogen in the human placenta where it appears in maximal concentration at the second to the third month of intrauterine life.

In 1929 it was possible to confirm the work of Lochhead and Cramer in regard to the presence of glycogen in the rabbit's placenta and to show that it had certain physiological properties distinguishing it from glycogen in the

liver (Huggett 1929). It is present at a maximum at the twenty-first day of pregnancy, falling off in concentration then and being present only in traces at full term (30 days in the rabbit). In this respect it contrasts with the human placenta where it is maximal at the second to third month in utero, though traces are still to be found at full term. It contrasts with liver glycogen in being independent of the content of sugar or endocrines in the blood and remarkably constant in percentage at any one fetal age. Szendi (1936) has shown that in both the rabbit and man the glycogen appears in peaks first in the decidua, then in the trophoblast, then in the fetal lung, and finally in the fetal liver. Corey (1935) has found in the rat the same independence of endocrines previously (Huggett 1929) found in the rabbit. Placental glycogen can be decreased only by agencies such as toxic doses of thyroxin or insulin which cause gross catabolism of the placenta and increased nitrogen excretion. It appeared to be part of the tissue of the body and bound up in the endogenous metabolism of the cells. Bernard had called the placenta a fetal liver. Needham (1931, p. 1025) analyzed other workers' results to show that the placental glycogen decreases after the peak period as the fetal liver glycogen increases, suggesting a constancy of glycogen in the developing ovum.

THROUGHOUT PREGNANCY.							
	FLOW.	FLOW PER Kg.	AVERAGE FOETAL WEIGHT DEPOSITED PER DAY.	FLOW PER GRAM DEPOSITED			
	ml/min.	litres.	grams.	litres.			
SHEER	130	130-250	27	5.5			
GUINEA PIG.	2.5	45-108	1.35	1.28			
MAN 93-94 DAYS	2.1	43.9	2.82	1.07			

Fig. 11.—Average umbilical blood flows during pregnancy. (From Huggett and Widdas: J. Physiol. 114: 306, 1951, Cambridge University Press.)

The most important step in the elucidation of the role of placental glycogen was achieved by Hoet (1953) who has shown that 0.5 mg. per day of cortisone given to rabbits will increase the quantity of placental glycogen in both the fetal and maternal portions and that at the same time the fetus puts on weight. Bigger doses cause abortion. This is the first occasion that a factor has been found which will cause increased placental glycogen and even more increased fetal growth.

## Fetal Carbohydrates-Blood Sugars

The identity of fructose in the fetal blood up till 1922 depended solely upon evidence of levorotation and the Selivanoff test. It was not until 1946 when Bacon and Bell isolated fructose from the blood of fetal sheep and ob-

tained its crystalline triacetone derivative that its identity was established. They, together with Cole and Hitchcock working in Cambridge under the inspiration of the late Sir Joseph Barcroft were able to show that fetal sheep blood contains fructose as well as glucose. Barklay, Haas, Huggett, King, and Rowley (1949) demonstrated that glucose averaged 20 to 40 mg. per cent in the blood of the sheep fetus but that the fructose was as high as 180 mg. per cent in each (fortieth day) fetal life and fell by full term to about 20 mg. per cent, though the amniotic and allantoic fluids might have much higher concentrations even up to over 900 mg. per cent. Similar results have been obtained in the cow by Matner, Chang, and Loefer (1951) (Figs. 12, 13, 14, and 15).

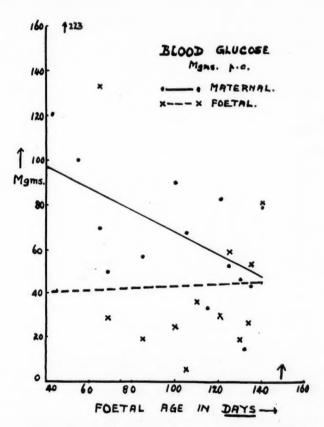


Fig. 12.—Blood glucose of pregnant sheep and fetus.

In 1938 Passmore and Schlossman demonstrated that when glucose was injected intravenously into the pregnant sheep and the sugar concentration followed simultaneously in the maternal and fetal blood the maternal hyperglycemia first exceeded the fetal blood sugar, which also rose, but subsequently the fetal hyperglycemia exceeded the maternal.

In the light of the subsequent findings in 1946 by Bacon and Bell that fetal sheep blood contained fructose, my colleague, Dr. F. L. Warren, suggested repeating the experiment of Passmore and Schlossmann but estimating the fetal blood for glucose and fructose simultaneously. This showed that intravenous glucose in the pregnant ewe gave a hyperglycemia half an hour later in the fetus. But simultaneously as the glucose fell in the fetal blood the

fructose from the beginning of the experiment slowly and steadily rose to about 200 mg. per cent and this fetal hyperfructosemia lasted as long as 6 to 10 hours (Fig. 16). The same result was produced by injection into the fetus—a fetal hyperglycemia subsiding relatively soon and a slow-rising long-lasting hyperfructosemia. With the fetal hyperglycemia there was evidence of back flow of glucose to the mother (Fig. 17).

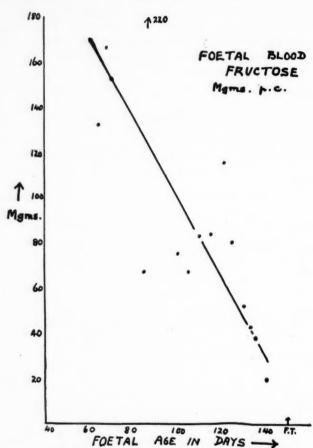


Fig. 13.—Blood fructose of fetal sheep.

If fructose was injected into the fetus it did not go back to the mother, nor was there evidence of this return of fructose at any other time though, as has been said, glucose can reverse from fetus to mother if injected into the fetus.

Fructose appears to be formed solely by the placenta and never by the fetus. This is known for two reasons:

A. If we produce experimental hyperglycemia in twin fetuses and detach one immediately afterward, hyperfructosemia occurs in the attached fetus but the fructose falls in the detached fetus (Fig. 18).

B. If we replace the detached fetus by a pump having produced maternal hyperglycemia and perfuse the placenta in situ we obtain hyperfructosemia in the placental pump circulation (Fig. 19).

It was possible to show that the sheep's placenta forms fructose from glucose at normal blood glucose levels and does not require any hyperglyce-

mia. This was done by very slowly injecting the mother with radiocarbon in glucose. Under the conditions radioactive fructose was formed in the fetal blood as is shown in Fig. 20A though there was no rise of blood sugar as shown in Fig. 20B.

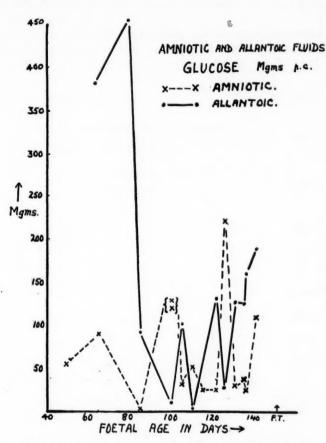


Fig. 14.—Glucose content of amniotic and allantoic fluids.

It is possible to detach the fetus after cannulating the umbilical veins and arteries and joining the cannulas to a pump (Henry-Jouvelet pump) and perfusing the placenta. Two techniques of perfusion have been utilized:

A. Recirculating perfusion, in which the effluent fluid goes to a reservoir from which the pump sends it back to the placenta. This permits a condition of equilibrium to be observed.

B. "Through" perfusion, in which the effluent fluid goes to a separate reservoir and never returns to the placenta. It traverses only once. This permits a measure to be made of substances formed or removed from the perfusion liquid.

The fluid used has been both blood and plasma (heparinized), most often plasma derived from either the maternal blood or another sheep. The preparation preserves its condition longer on plasma.

Fig. 21 shows the two perfusion techniques employed.

The technique of recirculating perfusion has been used to show that the level of fructose in fetal blood falls if cut off from the placenta but goes on

rising in the perfused placenta. We can do a recirculation perfusion in the placenta of a sheep fetus (Fig. 22) and on infusing glucose into the mother the placental glucose rises steeply and falls when the maternal falls but the fructose rises less steeply but is longer lasting. The placenta-pump preparation therefore behaves as does the intact placenta and fetus to infusion of glucose.

When we through-perfuse the placenta (Fig. 23) with plasma and collect the effluent and measure the glucose and fructose produced by the placenta we find that if we increase the maternal blood sugar experimentally

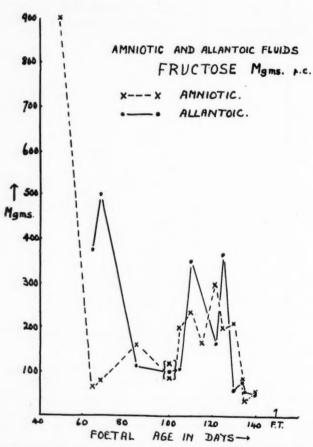


Fig. 15.-Fructose content of amniotic and allantoic fluids.

there is an increased collection or formation of glucose by the placenta from about 10 to 12 mg. per minute to 70 to 80 mg. per minute. But the fructose collection is unaltered at about 10 mg. per minute despite the rising of the maternal blood sugar from 70 mg. per cent to 670 mg. per cent.

If instead of raising the maternal blood glucose ten times in value we raise the perfusing placental glucose (Fig. 24) we find as in the last experiment that the fructose collection proceeds at the same rate as previously but the glucose collection is reversed into a glucose loss to the placenta and mother as judged by the rise of maternal blood glucose concentration.

It is clear therefore that the rate of production of fructose by the placenta is a constant and independent of the level of glucose in the maternal or fetal

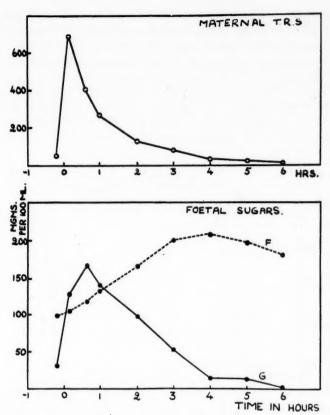


Fig. 16.—Sheep 238. Pregnant. Fetal age 115 days. Glucose injected intravenously into the mother 2 Gm. per kilogram of maternal body weight.

O O Maternal T.R.S. ( = glucose)

Fetal glucose
Fetal fructose
(From Huggett, Warren and Winterton: Nature 164: 271, 1949.)

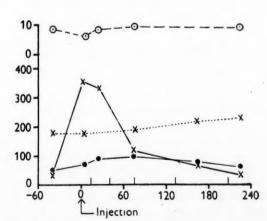


Fig. 17.—Sheep 223. Fetal age 93 days. Glucose injected intravenously into an umbilical vein, 1.0 Gm. per kilogram of fetal body weight.

O O Maternal blood T. R. S. (glucose), milligrams per 100 ml.

Fetal blood fructose, milligrams per 100 ml.

Fetal blood hemoglobin, grams per 100 ml.

bloods, that it goes on independently of the direction of flux of the glucose, but as shown by the C<sup>14</sup>-glucose experiments it ultimately comes from glucose, though other sources are not ruled out.

We were then curious to find out if the fructose utilization by the placenta was dependent on the blood fructose or glucose levels.

Sheep 646 was therefore perfused by recirculation and the umbilical blood fructose was elevated initially to 150 mg. per cent by injection of fructose into the reservoir. During the next hour the placental fructose steadily fell from 155 mg. per cent to 120 mg. per cent.

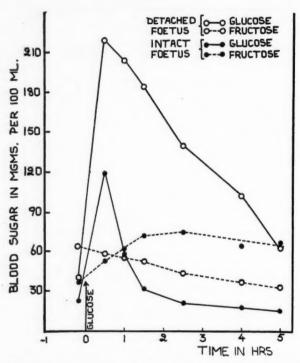


Fig. 18.—Sheep 224. Fetal age 135 days. Twins. Glucose infusion into both fetal circulations. One fetus detached immediately after, second left intact.

• Glucose in attached fetus

o Glucose in detached fetus

(From Huggett, Warren and Winterton: Nature 164: 271, 1949.)

After one hour the maternal blood glucose was raised from 50 mg. per cent to 450 mg. per cent. Immediately the placental glucose rose too as was expected, and as was to be expected the fructose concentration also rose as is practically always found when glucose is increased in concentration. Now since fructose concentration is the balance of placental formation and placental utilization and since this formation proceeds independently of the glucose concentration it follows that the utilization must be depressed by the rise of blood glucose. That is to say, the placenta can utilize both glucose and fructose but its utilization of fructose is inhibited by an increase in concentration of glucose which is utilized preferentially. This observation on the placenta fits in with Mann's (1951) finding upon the utilization of glucose and

fructose by the spermatozoon, that when only one sugar is present spermatozoa utilize either glucose or fructose with equal avidity. But if both are present then the spermatozoa utilize glucose in preference to fructose.

It is permissible to consider here certain of the implications arising out of these experiments. There are four major problems posed by them, the manner of passage of glucose and fructose across the sheep placenta, the origin or source of fructose, the relation of glycogen to fructose (if any), and finally the relation of these problems to growth in the fetus.

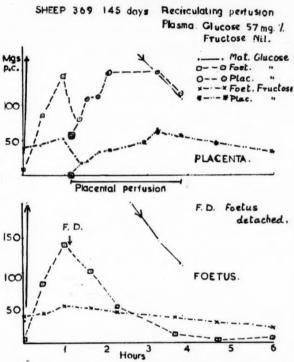


Fig. 19.—Sheep 369. Fetal age 145 days. Twin FR or FL. Glucose injected intravenously into mother. Umbilical cord FR cut and placenta PR perfused with heparinized plasma containing no fructose but 57 mg. glucose per 100 ml. Subsequent sugars estimated in detached fetus FR and in placenta-pump circulation PR. Fetus FL ignored, being left intact. FR and PR, right-hand fetus and placenta; FL, left fetus.

The distribution of fructose has been considered by Goodwin (1952) in the School of Veterinary Medicine at Cambridge. He finds it present in all Ungulata he examined but absent in rodents and carnivora. These findings agree with ours. We have also found it in the fetus of the fallow deer (Alexander, Huggett, Nixon, and Widdas 1953). In the case of human beings the fetal blood appears by the tests we have used to have no fructose. This is in agreement with Karvonen (1949). On the other hand Hagermann and Villee (1952) find human fetal blood has up to 4 to 5 mg. per cent of fructose but the large bulk of its blood sugar is glucose. This finding is confirmed by Wallenfels (1952). Despite this finding, however, the phenomenon of fructose in human fetal blood is different from its presence in the blood of the sheep and the ungulates where it is present in larger quantities and in preponderance over

glucose. Fructose will not return across the placenta to the mother if injected into the umbilical circulation; it appears more slowly in fetal blood when injected into the maternal blood. If radioactive glucose is injected into the maternal blood both glucose and fructose increase in the fetal blood, the

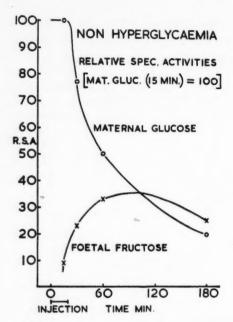


Fig. 20A.—Maternal and fetal blood sugar concentrations with the slow intravenous infusion of radioactive glucose into the mother.

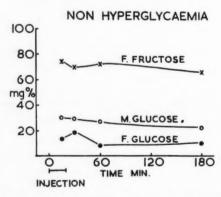


Fig. 20B.—Relative specific activities of the maternal and fetal blood sugars.

glucose the more rapidly. But radioactivity appears some half hour later in the new fetal fructose than in the new fetal glucose. If fructose is injected into the maternal blood in the same dose as glucose it rises more slowly in the fetal blood than the glucose.

All experiments show its production and passage out of placental cells into the fetal (umbilical) blood is by a different process from that of glucose with one exception. When a very high dose of fructose is put into the mater-

nal blood in the first five minutes the fetal fructose rise parallels that of glucose but then it slows up. In that first five minutes we regard the passage of the two sugars as being similar.

Widdas (1952) has analyzed the kinetics of hexose passage across the placenta and has shown that it is neither for glucose nor fructose capable of explanation on a diffusion basis. He hypothesizes an active transport mechanism carrying the glucose molecules. Without giving the full evidence it is possible to draw the attention to the fact that after injection of glucose into the maternal blood the resultant fetal hyperglycemia never equilibrates but begins to fall even when a positive gradient exists between the two blood sugar concentrations and the fetal blood should rise still further to equilibration. On the other hand the slow-produced fructose will continue to rise so that after some two, three, or four hours it comes to exceed in concentration both the fetal blood glucose and the maternal blood glucose. The chemical nature of the active carriers is unknown. There are various physicochemical reasons why Widdas is reluctant to look on them as phosphate esters.

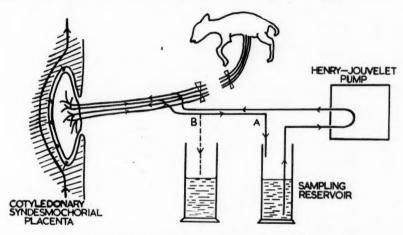
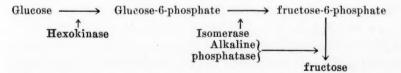


Fig. 21.—Diagram showing techniques of placental perfusion.

The carriers for fructose transport would appear to be different from those for glucose transport except in the rare experimental condition when the maternal blood is saturated with glucose.

The degree to which the knowledge of sugar metabolism in liver and muscle can be applied to the glycogen, glucose, fructose story of the placenta is difficult to assess till more work has been accomplished. The problem is to explain glycogen being found in quantity in the rodent and human placenta, glucose being converted to fructose, and free fructose appearing in the fetal blood of sheep.

One obvious path for fructose formation is



Hexokinase has not been found though isomerase has been extracted from the sheep's placenta but its conditions of activity and equilibrium do not explain the in vivo production of fructose from glucose (Parr and Warren 1951). On the other hand Wajzer and Zelnik (1951) got aqueous extracts of the human placenta which will hydrolyze 30 per cent of glucose-6-phosphate to fructose-6-phosphate. But as has been said earlier in this lecture human fetal blood possesses only a trace of fructose (Hagermann and Villee 1952). Wajzer and Zelnik also found their placental extracts showed no evidence of in vitro hexokinase activity unless adenosine triphosphate (ATP) was added. This, however, apparently is absent in the human as well as the sheep's placenta.

### 22.4.52 SHEEP No. 644.

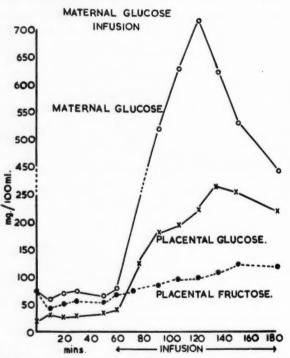


Fig. 22.—Recirculation perfusion of the placenta, recording equilibrium between mother and fetus. Maternal glucose infusion yields net of placental glucose and of placental fructose.

Warren and his colleagues (Ainsworth, Parr, and Warren 1951) have investigated the distribution of alkaline phosphatase. This is present in almost all types of placenta but paradoxically is in maximal concentration in those types which do not produce fructose and minimal in the ruminant species which do make fructose. Fahmy (1953) has looked at the histochemical distribution of glycogen and the phosphatases in placentas and fetuses of different species. He finds alkaline phosphatase is in the sheep in the maternal parts of the placenta but absent in the chorionic villi and other fetal parts. In the last ten days of sheep pregnancy it goes from the maternal cells covering the placenta between the villi but appears in the endothelium of the mater-

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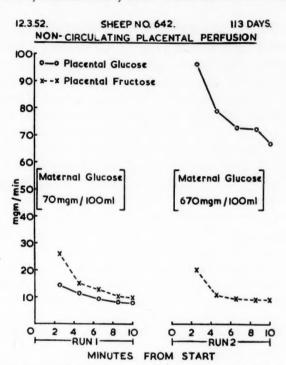
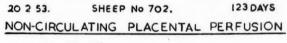


Fig. 23.—Through perfusion of the placenta at low (70 mg. per cent) and high (670 mg. per cent) maternal blood sugar, recording sugar collections in milligrams per minute. Fructose collection unaltered by high glucose, glucose collection increased.



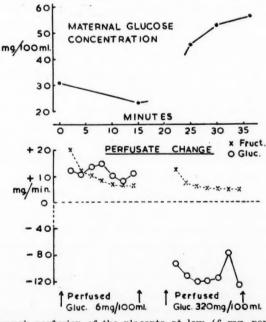


Fig. 24.—Through perfusion of the placenta at low (6 mg. per cent) and high (320 mg. per cent) concentration of perfusing placental glucose. Fructose collection unaltered at 8 mg. per cent but maternal glucose concentration raised by back flow across the placenta, the gain of 8 mg. glucose per minute being converted to a loss of 120 mg. per minute.

nal blood vessels. In the human placenta, however, alkaline phosphatase is absent in the maternal parts of the placenta but present in the fetal syncytio-trophoblast accompanied by large numbers of mitochondria. In the human placenta practically no fructose is produced. Fahmy finds that in all species examined glycogen is never present in the same cells in which alkaline phosphatase is demonstrable. Alkaline phosphatase is associated with high cellular activity as evidenced by the presence of mitochondria; glycogen is never present in the cells. This bears out the views of Dempsey and Wislocki (1944) that the deposition of glycogen in the placenta is related inversely to the metabolic activity of the cells in which it appears. When alkaline phosphatase is in the maternal tissue of the placenta then, and only then, do we find free fructose being liberated in quantity into the fetal blood. If it is in the chorionic villi it does not appear to liberate fructose in quantity and glycogen can accumulate in the less active cells of the placenta.

Villee (1953) in an important paper has shown that human fetal livers are unable to store glucose as glycogen till about the twentieth week of development but glycogen is known to be present in the human placenta before this. In vitro experiments showed placentas can produce glucose but it is a decreasing function with aging of the placenta. He has also investigated some of the possible substances from which glucose can be formed.

In regard to the function of fructose we know from the work of Dickens and Greville (1932) that aerobically placentas and fetal tissues of all species will consume fructose but anaerobically only the placentas of the cat, ferret, and man will utilize fructose. Once again the irony is that these species do not have any fructose to speak of in their fetal blood. There are three recent developments of our knowledge of glycogen and carbohydrates which need to be discussed here. There is the description of maltulose as a breakdown product of fetal liver glycogen of rabbit by Peat, Roberts, and Whelan (1952). Since maltulose contains fructose, this would be a link between rabbit glycogen and ruminant fructose. The work needs confirmation and extension. There is further evidence brought forward by Hoet (1953) that cortisone given to rabbits in doses of 0.5 mg, increases placental glycogen from the fifteenth day onward but in doses of 2.0 mg. causes abortion. He has found also from the fifteenth day a decreased sugar tolerance which results in hyperglycemia which however is decreased by cortisone. The whole phenomenon is linked with human liability to pregnancy diabetes.

For some years Young and his school in London and Cambridge have studied the relation of pituitary growth hormone and the metabolism of carbohydrates and protein. Their views are best set out in the paper he gave at the nineteenth International Physiological Congress in Montreal (Young, 1953).

Put briefly, the diabetogenic and growth hormones are identical. Administration to animals causes hypoglycemia unless growth is occurring when the hypoglycemia is diminished or nonexistent and nitrogen with carbon and hydrogen is stored as protein in newly formed tissue. Growth hormone among a number of actions also stimulates insulin to cause tissues to take up

amino acids. In fact, insulin may have its main action in the fixation of nitrogen with carbon and hydrogen. This finding of Young and his school fits in with the finding of Luetscher (1942) that individuals with untreated diabetes have high blood concentrations of amino acids and low glycine tolerances. Further insulin lowers both the blood sugars and the blood amino acids and increases glycine tolerance pointing to increased uptake of nitrogen, carbon, and hydrogen by tissues under the influence of insulin.

It appears, therefore, that in the pregnant animal we have a condition in which fixation of nitrogen, carbon, and hydrogen is occurring. This takes place both in the developing ovum and without in the maternal tissue and at considerably different rates in different species. There is evidence of overactivity of the anterior pituitary during pregnancy though as yet no absolute proof of increased production of growth hormone. There is the now classical fact of more cortisone production during pregnancy. Within the picture of growth involving fixation of nitrogen and carbohydrates, we have smaller cycles proceeding. Of these the placental growth and senescence is that upon which we need to focus. It is already known to be an organ competing with, if not transcending so far as the fetus in concerned, the liver and pituitary gland. During its growth it produces a pattern of carbohydrate metabolism different in different species. In all there is the common appearance of phosphatases, both acid and alkaline.

In the sheep and goat alkaline phosphatase is in the maternal parts of the placenta, in rodents and man it appears in fetal parts, notably in the syncytic-trophoblast of the villi, and is absent in the maternal parts. In the ruminant there is a large production of fructose by the placenta, which big production is almost absent in all other mammals. They, on the other hand, differ not only in the alkaline phosphatase being fetal in location but also in the production by the placenta of glycogen which seems to be present in the most active cells yet never in cells in which alkaline phosphatase can be found.

In the toxemias of pregnancy for which no cause can yet be found we have something common to all types and species. This is the aggravation of the condition by dietetic protein and alleviation in varying degree by carbohydrate.

In conclusion, therefore, it is hoped the picture of a pattern throughout mammalian pregnancy and intrauterine growth will help those following in the footsteps of Joseph Bolivar DeLee.

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# THE USE OF TANTALUM MESH IN CYSTOCELE WITH CRITICAL REPORT OF TEN CASES

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THE use of tantalum mesh in the repair of cystoceles was conceived when such favorable reports of its application under adverse circumstances for the repair of ventral and inguinal hernias appeared in the literature. Stafford and Morrow Peported success in repairing a herniation of the bladder following a retropubic prostatectomy and three previous unsuccessful attempts at repair of the resulting incisional hernia. In their case, the tantalum mesh was placed in direct apposition to the bladder. Goldberger and Davids have successfully used tantalum plates in the treatment of stress incontinence with no adverse effects. Koontz found that tantalum mesh could be used next to the intestine if peritoneum was lacking. Although there are numerous recognized procedures for the correction of cystoceles, there is still a significant rate of recurrence; therefore, a trial use of tantalum mesh was considered justifiable.

Published reports did not lead us to believe that serious consequences should develop from the use of tantalum mesh. According to Olson,<sup>17, 18</sup> tantalum is completely inert to any chemical that can be produced by the body and no foreign body reaction is produced. No electrolytic action will occur if an all-tantalum setup is used. Koontz and Kimberly<sup>19</sup> found that fibrous tissue starts growing around and through the mesh immediately after its implantation. Fibrosis is complete in about two weeks but is not profuse; it becomes more profuse with time, however, and is very dense at the end of two months. Further, Koontz<sup>20</sup> found that, under ordinary conditions, tantalum mesh does not migrate from the site in which it is implanted and that it could be used with impunity in the presence of infection if nonabsorbable sutures are not used with it. Soft pliable wounds resulted invariably. Wounds healed by granulation in cases in which the mesh was exposed by a slough of the surface tissues.

#### Selection of Patients

Ten patients were selected for the proposed procedure. In each case, the cystocele was sufficiently large to put the procedure to a real test. These patients had a variety of symptom and physical findings.

With regard to symptoms (Table I), 7 patients complained of a mass protruding from the vagina; 5 were conscious of a bearing-down sensation or heaviness in the pelvis; 4 had experienced such difficulty in initiating urination that digital replacement of the bladder was necessary; 4 had noted episodes

of urinary frequency while only 2 had complained of urgency; 2 had stress incontinence; one had had two episodes of complete urinary retention, requiring catheterization; and fecal incontinence was an associated symptom of one.

TABLE I. SYMPTOMS

Vaginal protrusion	7
Bearing-down pain	5
Urinary retention	5
Partial	4
Complete	1
Urinary frequency	4
Urinary urgency	2
Stress incontinence	2

As stated in Table II, these patients had a marked cystocele and each had a rectocele. Three had a complete prolapse of the uterus. In one, the cervix was hypertrophied and so elongated that it projected 3 inches beyond the introitus. Four had cervical stumps with partial prolapse in three. One had had a complete hysterectomy; one had a complete perineal laceration.

TABLE II. PELVIC PHYSICAL FINDINGS

Cystocele, large	10	
Rectocele	10	
Relaxation of pelvic floor	9	
Complete uterine prolapse	3	
Partial uterine prolapse	1	
Partial prolapse of cervical stump	3	
Complete perineal laceration	1	

## Technique

In our technique, the cystocele is repaired first by using the Kennedy plication technique<sup>21</sup> with regard to exposure, mobilization, and plication of the urethra and bladder (Fig. 1). Then a piece of cardboard or x-ray film is cut and trimmed with scissors as a pattern until it will lie in contact with the undersurface of the repaired bladder and urethra. It is cut to extend as far posteriorly as the anterior vaginal fornix and as far anteriorly as the junction of the middle and posterior thirds of the urethra. Laterally, it extends under the reflected vaginal walls into the paravesical spaces. Type 50 tantalum mesh with 0.003 inch wire is then cut approximately one-fourth inch larger than the pattern along all edges. The edges of the mesh are folded back so that the final size conforms to the original pattern. The folded edge gives added strength and facilitates handling and suturing. Anchoring sutures of Ethicon braided tantalum No. 000 are then placed at each corner. The two posterior sutures anchor the mesh to the cardinal ligaments and the two anterior ones to the periosteum of the median surface of the pubic rami if possible. After the tantalum insert is in place (Fig. 2), the excess vaginal wall

TABLE III. OPERATIONS PERFORMED

Cystocele repair and tantalum mesh insert	10
Rectocele repair	10
Perineorrhaphies	9
Vaginal hysterectomies	5
Excision of cervical stump	3
Repair of complete perineal laceration	1

is excised and is approximated in the midline with interrupted chromic No. 00 sutures. A loose iodoform pack is allowed to remain in the vagina for five days. A Foley catheter in the bladder is in place for the same period of time.

In addition to this, the 10 patients had a variety of other procedures performed (Table III). All had posterior colporrhaphies and perineorrhaphies. Five had vaginal hysterectomies; 3 had removal of the cervical stump; and one had a repair of a complete perineal laceration.

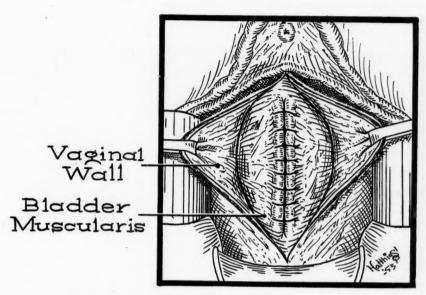


Fig. 1.—A conventional Kennedy plication technique for cystocele repair. The anterior vaginal wall has been incised along the midline. The bladder and posterior urethra have been mobilized and plicated with interrupted sutures.

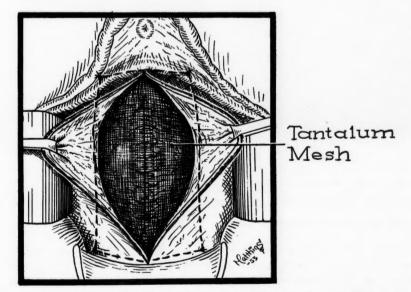


Fig. 2.—The tantalum mesh is anchored in place between the bladder and posterior urethra and the vaginal wall. Although pictured as roughly rectangular in shape, the pattern for the mesh is usually more trapezoidal with the anterior dimension shorter than the posterior dimension.

## Case Reports

CASE 1.—A 60-year-old gravida iv, para iv, was admitted to the hospital on May 6, 1953. She stated that a partial uterine prolapse had been present for 40 years. In 1950, she had an unidentified tumor removed from the bladder. Shortly after that, in 1950, she had a subtotal abdominal hysterectomy for "tumors of the uterus." Routine urethral soundings for three years by a urologist had been done, the patient remaining asymptomatic. Six weeks prior to her admission, she had experienced acute urinary retention which did not recur after a single catheterization until one week prior to admission. A Foley catheter was placed in the bladder and, finally, she was referred to Jefferson Davis Hospital on May 6, 1953.

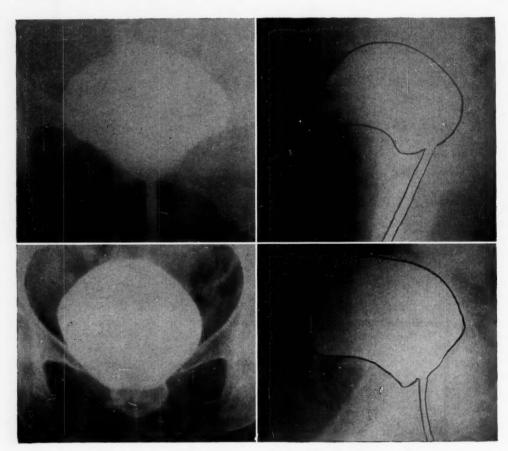


Fig. 3.—(Case 1.) A 60-year-old Negro woman suffering from partial prolapse of a cervical stump, urinary frequency and urgency, and complete urinary retention.

- A, Anteroposterior view before treatment with typical funneling of the bladder neck.
- B, Lateral view before treatment.
- C, Anteroposterior view after treatment with elevation of the bladder neck. The tantalum mesh is correctly placed and anchored in apposition to the bladder and posterior urethra.
  - D, Lateral view after treatment with the tantalum mesh in place.

Cystoscopy and intravenous pyelography were essentially negative, the exception being mild blunting of the renal calyces. On admission, the Foley catheter was removed, whereupon she was capable of spontaneous voiding but complained of marked urinary urgency and frequency. The cervix was elongated and protruded from the introitus. She had a marked rectocele and cystocele. She refused surgery and was dismissed May 11, 1953, but reconsidered and was readmitted and operated upon on May 19, 1953. The cervical stump

was excised and the cystocele repaired with tantalum mesh incorporated between the layers of the closure. The rectocele was also repaired. Her postoperative course was satisfactory. The anterior edge of the tantalum mesh was palpable along the midline but could not be visualized with the patient in the Sims position. This has been covered by granulation tissue. The patient is most apprehensive, complaining of a vaginal discharge, and marked urinary urgency and frequency. Cystoscopy, urinalysis, vaginal smears, and vaginal inspections have remained negative.



Fig. 4.—(Case 2.) A 70-year-old white multiparous woman suffering from a complete uterine prolapse.

A, Anteroposterior view before treatment showing the marked bladder descensus. A soft rubber catheter outlines the urethra.

B, Lateral view before treatment with the posterior urethrovesical angle preserved in spite of marked descensus of the bladder.

C, Anteroposterior view after treatment. The bladder is well elevated with the tantalum mesh in place. Lateral mobilization of the bladder is not complete and the tantalum is anchored anteriorly into the vaginal muscularis laterally.

D, Oblique view after treatment.

CASE 2.—A 70-year-old white gravida vii, para vii, was admitted to the hospital on March 7, 1953, with a complete uterine prolapse and marked cystocele and rectocele. She had sought medical attention because of an ulceration of the prolapsed posterior vaginal mucosa. Uterine prolapse had been complete for one year during which period she had

experienced occasional urinary frequency and constipation. Suprapubic discomfort had been noted for one month on urination. Measures were instituted to clear up the vaginal ulceration, including estrogens locally and a ring pessary. Cystograms and cystoscopy revealed multiple large bladder diverticuli. On March 31, 1953, a vaginal hysterectomy and anterior and posterior colporrhaphy were done, utilizing tantalum mesh in the anterior repair. Her postoperative course was satisfactory. Slight stress incontinence was noted initially after she went home but this soon abated, leaving her symptom free. On follow-up examination, the vaginal vault was very well supported; there was no evidence of recurrent cystocele; and the vaginal epithelium was soft and pliable.

TABLE IV

CASE NO.	AGE	GRAVIDA PARA				RESULTS	
				IM	IMN	IEDIATE	
			CONDITION	SUPPORT	ANTERIOR VAGINAL WALL	FINAL	
1	60	iv	iv	Prolapse of cervical stump; acute uri- nary retention; marked cystocele and rectocele	Excellent	Slight surface slough	Excellent; vaginal wall intact
2	70	vii	vii	Complete uterine prolapse; marked cystocele and rectocele	Excellent	Intact	Excellent
3	70	Multipa	rous	Prolapsed cervical stump; marked cystocele and rectocele	Excellent	Intact	Excellent
4	41	v	v	Marked cystocele and rectocele	Excellent	Moderate surface slough	Excellent sup- port; granu- lation cover- ing vaginal wall defects
5	71	v	v	Cervical stump; marked cystitis; chronic pyelonephritis; marked cystocele and rectocele	Good	Mild partial slough	Good support; defects cov- ered; vagina soft and pliable
6	46	iv	iv	Complete uterine prolapse; marked cystocele and rectocele	Excellent	Intact	Excellent
7	40	i	i	Previous total hys- terectomy: marked cystocele and rectocele	Excellent	Intact	No follow-up
8	48	i	i	Prolapsed cervical stump; marked cystocele and rectocele	Excellent	Slight surface slough	Excellent with vaginal wall intact
9	64	ii .	ii	Complete uterine prolapse; marked cystocele and rec- tocele; healed third degree perineal laceration			Excellent
10	45	i	i	Partial uterine prolapse; multiple leiomyomas; marked cystocele and rectocele	Excellent	Intact	Excellent

## Results

Nine patients reported for follow-up examinations and there were no recurrent cystoceles. The anterior vaginal walls were well supported and there was no appreciable sagging when straining occurred. Urethral soundings demonstrated good vesicourethral angles with no angulation of the urethra or constrictions of the urethral lumina. Postoperative cystograms on two patients revealed well-supported bladders with continued maintenance of the posterior urethrovesical angles. Cystograms were usually made in accordance with the technique described by Jeffcoates and Roberts<sup>22</sup> (Figs. 3 and 4).

In 5 cases (Table IV), the anterior vaginal walls remained completely intact, each of these remaining soft and pliable in the operative site. In 4, the tantalum mesh was exposed. In one, an elderly woman of 60, a few spicules of the anterior edge of the mesh were palpable but could not be visualized; an infection of the anterior vaginal incision occurred postoperatively but responded nicely to antibiotic and estrogenic therapy. In two others with exposed mesh, the exposed area was trimmed with suture scissors. The last of the four was not trimmed. In all four, continued improvement has been evident with gradual coverage of the mesh by granulation tissue.

Of the 10 patients, 5 were not interested in coitus because of age or the lack of a spouse; 3 others have found coitus satisfactory; one has not attempted coitus because of a fractured cervical vertebra in an accident soon after operation; and the last patient, aged 44, has failed to report for follow-up examination.

Two patients have experienced recurrent urgency and frequency of urination; one of these 2 patients had originally a recurrent cystitis of three years' duration. The repair of the large cystocele was done to facilitate clearing up this recurrent infection. At the time of follow-up examination, the cystitis had recurred and the mesh was partially exposed through the anterior vaginal wall. Marked improvement occurred with antibiotic therapy. Cystograms revealed a well-supported bladder and maintenance of a fairly good posterior urethrovesical angle with straining. The other patient complained bitterly of urgency and frequency of urination and a persistent vaginal discharge in spite of urinalyses, cystoscopic, neurological, and vaginal examinations and smears, all of which remain normal. No cause can be found to explain her symptoms. The apprehension she exhibits leads us to think her complaints may be functional.

In no instance did a genitourinary fistula develop or the mesh erode into the lumen of the urethra or bladder. None of the patients have developed stress incontinence of urine, whereas the 2 who listed this as one of their original complaints were cured.

#### Summary

This is a preliminary report of the use of tatalum mesh gauze to supplement the conventional Kennedy-type plication technique for the correction of cystoceles. In each case, the cystocele was sufficiently large to put the procedure to a real test. The tantalum mesh was not used with the intent of offering immediate support to the repair as a hammocklike sling but to offer eventual support by the additional fibrous tissue which would be formed in and about the mesh.

Follow-up examinations over a period of from six to eighteen months in 9 cases revealed no recurrent cystoceles. The only adverse finding attributed

to the mesh was the sloughing of areas of the superficial vaginal wall in 4 cases with partial exposure of the mesh. This did not represent a serious problem. The exposed mesh was trimmed in two cases. Granulation tissue progressively is covering the defects in the vaginal wall.

We believe the slough occurred because, as in any plastic flap that sloughs, the circulation was not adequately maintained in the vaginal wall overlying the tantalum mesh. Ischemic necrosis undoubtedly occurred. Care should be taken to reflect the vaginal wall in its complete thickness, rather than split, to preserve good vascularity. A variation which we propose to use in the future is the technique of overlapping the vaginal muscularis as described by Bissell<sup>23</sup> (Fig. 5).

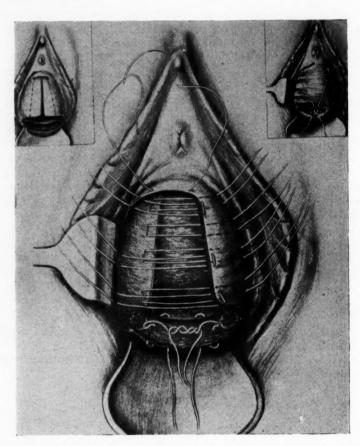


Fig. 5.—Technique of overlapping the anterior vaginal muscularis as described by Dougal Bissell in 1918.

We believe this closure will preserve the vascularity and reduce the possibility of ischemic necrosis.

We intend to continue to use tantalum mesh cautiously in the repair of cystoceles and in addition to operate upon a series of patients using lyophilized fascia lata for a study of comparative results.

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## Department of Case Reports New Instruments, Etc.

## INFECTIOUS HEPATITIS IN THE FIRST TRIMESTER OF PREGNANCY AND ITS EFFECT ON THE FETUS

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THE frequently tragic effect on the fetus of maternal rubella in the first trimester of pregnancy is well known. This has directed increasing attention to other virus diseases complicating pregnancy. At present, however, very little significant statistical information has been gathered for the other virus diseases, including infectious hepatitis.

Herewith are presented two cases of infectious hepatitis which occurred during pregnancy.

CASE 1 .- Mrs. E. K., a 25-year-old white Italian-American, para i, gravida ii, type O, Rh positive, Wassermann negative, whose last menstrual period was May 2, 1949, was admitted to the Methodist Hospital June 17, 1949, complaining of jaundice of ten days' duration. The past history was negative. The patient stated she was well until two weeks before admission at which time she developed nausea, anorexia, and noticed "burgundy-colored urine." For ten days prior to admission she had nausea and vomiting and was unable to keep solid food down. At this time she thought the scleras were "yellow." Five days before admission cutaneous icterus developed which increased in severity. For three days prior to admission she complained of a dull, nonradiating ache in the right upper quadrant and "black" but not tarry stools. There was no history of chills or fever. Admission examination revealed the temperature to be 100° F., pulse 80, respirations 20, blood pressure 100/60, weight 106 pounds, height 5 feet, 2 inches. The patient appeared acutely ill. Skin and scleras were icteric. Abdominal examination revealed right costal margin and right upper quadrant tenderness. The liver was palpable two inches below the costal margin and was extremely tender. A lower midline suprapubic mass extended one fingerbreadth above the symphysis. Positive pelvic findings were: marital introitus, gynecoid pelvis, and vellowish vaginal mucous membrane. The uterus was enlarged to six weeks' size, soft, anterior, and movable. Hegar's sign was positive. The right ovary was palpable and normal. The impression was: (1) infectious hepatitis; (2) six weeks' gestation.

Laboratory data on admission were: red blood cells 4.3 million, hemoglobin 14.6 Gm., white blood cells 7,800 with a normal differential, sedimentation rate 25, catheterized urine positive for bile. Blood chemistry findings were: nonprotein nitrogen 33, sugar 73, cholesterol 171, alkaline phosphatase 8 units, phosphorus 7.9, total protein 5.5, albumin 3.6, globulin 1.9, icteric index 200, van den Bergh delayed reaction positive, and cephalin

flocculation test 2 plus. Chest plate and flat plate of the abdomen were negative. The therapy instituted on admission was bed rest, fluid to soft diet, and Solu-B intravenously. She was gradually placed on a high-protein diet. Her hospital course was uneventful. Subsequent laboratory results were as follows: June 24, 1949; sedimentation rate 40, alkaline phosphatase 13.5 units, total protein 5.8, albumin 2.7, globulin 3.1, icteric index 200, van den Bergh delayed reaction positive, cephalin flocculation test 2 plus. June 26. 1949: zinc turbidity 14 units, phenol turbidity 22 units, thymol turbidity 7.9 units. July 2, 1949: urine negative, blood uric acid 2.4. July 5, 1949: alkaline phosphatase 8.3 units, total protein 6.3, albumin 3.6, globulin 2.7, icteric index 30, cephalin flocculation test 2 plus. July 12, 1949: red blood cells 4.1 million, hemoglobin 12.1 Gm., white blood cells 10,500, normal differential, urine negative, sedimentation rate 38, alkaline phosphatase 11 units, total protein 6.1, albumin 4.2, globulin 2.9, icteric index 20, van den Bergh test negative, cephalin flocculation test plus-minus. July 20, 1949: red blood cells 3.6 million, hemoglobin 10.8 Gm., white blood cells 11,600, normal differential, sedimentation rate 43, alkaline phosphatase 13.2 units, total protein 6.7, albumin 3.9, globulin 2.8, icteric index 12, van den Bergh delayed reaction positive, cephalin flocculation test plus-minus and urine negative. She was discharged on the thirty-fifth hospital day.

The remainder of her antepartum course was uncomplicated.

She was readmitted to the hospital on Feb. 2, 1950 (the estimated date of confinement was February 6), in active labor. The membranes ruptured spontaneously. After five and one-half hours of normal labor, a living female infant weighing 6 pounds, 4 ounces, was delivered spontaneously from the left occipitoanterior position with the aid of a median episiotomy.

Examination of the infant revealed a moderate right third- and seventh-nerve paralysis that has persisted to date.

The postpartum course was normal. Laboratory data revealed: red blood cells 4.5 million, hemoglobin 13.5 Gm., urine normal, alkaline phosphatase 4.6 units, total protein 7.0, albumin 4.3, globulin 2.7, icteric index 6, van den Bergh test negative, cephalin flocculation test negative, and phenolsulfonphthalein test normal.

CASE 2.-Mrs. T. M., a 37-year-old white American woman, para v, gravida ix, type O, Rh positive, Wassermann negative, whose last menstrual period was April 4, 1951, was admitted to the Lenox Hill Hospital, June 28, 1951, complaining of jaundice of one week's duration. Past history revealed "infectious arthritis" at 9 years of age and "jaundice" at 11 years of age. One week prior to admission the patient noted the onset of extreme fatigue. Two days later she noted pruritus and a yellowish tint to the eyes and skin, clay-colored stools, and dark urine. She complained of mild lower abdominal cramps. No history of recent infections, right upper quadrant pain, gall stones, or exposure to infectious hepatitis was given. Admission examination revealed a temperature of 100° F., pulse 82, respirations 20, blood pressure 92/56, weight 193 pounds. The skin and scleras were yellow. The left pupil reacted poorly to light and accommodation and was slightly larger than the right. The fundi were negative. Abdominal examination was difficult due to obesity but a lower midline mass extended to two and one-half inches below the umbilicus. Pelvic findings were: marital introitus, gynecoid pelvis, uterus enlarged coincident with dates, and a hypertrophied, lacerated cervix. The impression was: (1) acute hepatitis due to infection; (2) 11 weeks' gestation.

Laboratory data on admission were: red blood cells 4.2 million, hemoglobin 13.2 Gm., white blood cells 6,300, normal differential, sedimentation rate 83. Urinalysis showed a one plus albuminuria and was strongly positive for bile. Blood chemistry determinations showed serum bilirubin 10.2, alkaline phosphatase 4.5 units, and diastase 62. An electrocardiogram revealed a left axis deviation. A chest plate was negative. A flat plate of the abdomen revealed an enlarged uterus and was negative for biliary stones. The therapy commenced was bed rest and low-fat diet. Her course was afebrile. The jaundice gradually decreased. Her appetite improved and she was placed on a high-protein, high-carbo-

hydrate, and moderate-fat diet and vitamins. The liver remained enlarged to four finger-breadths below the costal margin. Further laboratory studies were: June 30, 1951: feces, trace of bile pigment, urea nitrogen 6.4, total cholesterol 135, free cholesterol 105, cholesterol ester 30, cephalin flocculation test 4 plus, thymol turbidity test 16 units, serum protein 7.4, albumin 4.4, and globulin 3.0. July 14, 1951: serum bilirubin 0.7. July 18, 1951: cephalin flocculation 2 plus, thymol turbidity 7.5 units.

The patient was discharged to the outpatient department on the twenty-second hospital day. The remainder of her antepartum course was uneventful and the liver receded to

two fingerbreadths below the costal margin.

She was readmitted on Jan. 5, 1952 (the estimated date of confinement was Jan. 11), in labor. The membranes ruptured spontaneously. Spontaneous delivery of a normal, living, 8 pound, 5 ounce, male infant occurred after a labor of two hours, fifty-three minutes. A first-degree laceration did not require treatment.

The postpartum course was normal. The cephalin flocculation test at this time was negative.

Subsequent follow-up of the infant has shown him to be normal although he was admitted Dec. 28, 1952, for bronchopneumonia and discharged well on the tenth hospital day.

### Comment

Infectious hepatitis complicating pregnancy is rare. Its incidence in the sporadic form is 0.02 per cent¹ whereas in epidemic form it is 0.85 per cent.² This low incidence has made it difficult to obtain accurate data concerning the effect of this virus upon the fetus, particularly during the first trimester, the organogenetic period of the fetus.

A perusal of the literature to date reveals the following sporadic reports in this regard. Gronvall and Selander's 10 cases of infectious hepatitis in the first trimester of pregnancy resulted in one infant with a cleft palate, one abortion, and eight normal infants. Kass reported a markedly hydrocephalic and microphthalmic infant in his one case. Kellogg and Wesp presented a case of infectious hepatitis which occurred about one month before conception with the patient remaining jaundiced for thirty-two weeks. This fetus was a composite monster. Ingerslev and Teilum, however, mentioned one case and Hartman and Kennedy noted two cases with delivery of normal infants following this complication in the first trimester.

On the other hand, Hellbrugge<sup>8</sup> reported a case in which the subsequent infant at 3 months of age showed physical and mental signs of retardation. These included developmental eye disturbances as follows: on the right, microphthalmus, congenital coloboma of the iris, the optic nerve, and the choroid; on the left, incomplete coloboma of the iris. In addition, microgyry with a simultaneous dilation of a part of the internal cerebral system was noted. A more recent report by Roth<sup>9</sup> included two cases of spontaneous abortions and one in which there was a normal term infant.

In regard to the hepatitis virus, whether these congenital abnormalities are the result of changes in oxygen metabolism of the embryo,<sup>8</sup> the blockade of plasma albumin,<sup>8</sup> or transplacental transfer of the virus is not known at this time.

The evidence for and against the transplacental transfer of the hepatitis virus is meager. Stokes and co-workers, 10 Bellin and Bailit, 11 Keller and

Nute,12 and Williams and Gaber13 offer evidence in its favor. Zondek and Bromberg, however, have concluded that the fetus in utero is not infected, either because the hepatitis virus does not cross the placental barrier or because it does not circulate in sufficient amounts.

Since the occurrence of rubella in the first trimester of pregnancy seems productive of so many fetal abnormalities and no effective therapy has been found to prevent these, therapeutic abortion has been advocated.<sup>14, 15</sup> Does ininfectious hepatitis in the first trimester, the so-called "organogenetic" period, constitute a menace to the fetus and justify such drastic action?

To date, 21 cases of infectious hepatitis in the first trimester of pregnancy have been reported (including the 2 presented here for the first time). Five of these have shown abnormalities and 3 patients have aborted. There may have been many cases of infectious hepatitis in the first trimester that were uncomplicated and not reported, however. If they were reported, the incidence of abnormalities might be within the expected range. It therefore behooves all obstetricians to report all cases of infectious hepatitis just before and during the first trimester of pregnancy. Conservative obstetrics must still be the treatment of choice in these cases and therapeutic abortion is not indicated a this time.

## Summary

- 1. The literature on maternal infectious hepatitis during the first trimester of pregnancy and its effect on the fetus have been reviewed.
  - 2. Two more cases have been added to the literature.

Acknowledgement is made to the Department of Obstetrics and Gynecology of the Lenox Hill Hospital for permission to present Case 2.

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  - 130 EIGHTH AYENUE

## A TUBAL PREGNANCY IN THE SECOND TRIMESTER

## Case Report

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THE literature is replete with reports of tubal pregnancy. The differential diagnosis of ruptured ectopic gestation has been frequently discussed. Less has been written, however, regarding full-term tubal pregnancy, and only nine pathologically documented cases have been reported.¹ Tubal gestation in the second trimester is likewise unusual. Review of the literature over the past ten years discloses that only three cases have been reported as such.²,³,⁴ Therefore, we feel that the following case will be of interest because of the diagnostic problems presented.

The patient was a 35-year-old, para ii, gravida iv, married Negro woman, who was first seen in the antepartum clinic on July 15, 1953, at which time she stated that her last menstrual period was on March 27, 1953.

Previous pregnancies included a spontaneous delivery, elsewhere, of a 10 pound infant after twelve hours of labor; and in 1951 the patient delivered spontaneously a 9 pound infant after nineteen hours of labor. This latter pregnancy was complicated by mild pre-eclampsia with blood pressure ranging from 140/75 to 140/100. There was occasional 1 to 2 plus albuminuria. In January, 1953, the patient had a left tubal pregnancy of, approximately, six to eight weeks duration, treated at another hospital by laparotomy and left salpingo-oophorectomy. This tubal pregnancy had ruptured and she was admitted in shock and required 1,000 c.c. of whole blood.

The patient's weight was 210 pounds, blood pressure 130/84. General physical examination was negative except for moderate obesity and a well-healed suprapubic midline incisional scar. Pelvic examination revealed that the uterus was enlarged to three finger-breadths below the umbilicus; the adnexa were described as being clear. A hemoglobin determination at that time revealed 9.3 Gm. per 100 c.c. of blood. Urinalysis was negative, as were the Mazzini test and the cervical and urethral smears for Neisseria; the blood group was A, the Rh factor negative. The husband's blood had been found to be Rh positive on a previous determination.

The patient had previously registered for this pregnancy with the antepartum clinic of another hospital. At that time an Aschheim-Zondek test was taken and found to be positive. From that time on the pregnancy was unremarkable, except for mild morning nausea and vomiting, until the morning of July 4, 1953, when she experienced a sudden onset of sharp right lower quadrant pain, which was steady and not accompanied by nausea or vomiting, chills, fever, or vaginal bleeding. She also admitted to frequent bouts of cold sweats and weakness following the onset of this pain. There was no history of shoulder pain. She presented herself to the emergency department of the other hospital of registry, where examination revealed an acutely distressed patient with normal vital signs. Significant physical findings included an abdomen which was markedly tender in the right lower quadrant with referred rebound tenderness to the left. On pelvic examination the cervix was described as being closed and soft. An exquisitely tender mass,

movable, fluctuant, and approximately 5 cm., in size, was described as lying in the cul-desac and thought to be arising from the right adnexal region. It was the impression of the admitting physician that the patient had an intrauterine pregnancy with a twisted prolapsed ovarian cyst but that ectopic pregnancy should be considered.

Admitting laboratory data included a negative urinalysis and a hemogram which showed hemoglobin 9 Gm., red cell count 3.1 million, white count 9,300. The differential was normal. A chest x-ray was read as negative.

The patient was placed on bed rest and mild sedation. Her course in the hospital was unremarkable with periodic blood pressure readings stable between 90/60 and 110/70. No change in findings from those on admission was noted on repeat pelvic examination by other observers. A flat plate of the abdomen taken on July 6, 1953, was interpreted as being negative. The abdominal symptoms and signs subsided and hemoglobin values remained stable. She was discharged on July 7, 1953, with a final diagnosis of intrauterine pregnancy and suspected twisted prolapsed ovarian cyst, to be followed in the antepartum clinic of that hospital.



Fig. 1.—Preoperative roentgenogram of the abdomen. A symmetrical mass may be seen arising out of the true pelvis. The fetal skeleton is extrinsic to this mass.

The patient was next seen at the Sloane antepartum clinic on Aug. 12, 1953, for her routine examination, at which time the uterus seemed to be enlarged to one fingerbreadth below the umbilicus. Other physical and laboratory findings were unremarkable and she was asked to return in one month.

She was next seen in the admitting emergency clinic on Sept. 2, 1953, at which time she complained of constant left lower quadrant pain of one day's duration. There was some nausea but no vomiting. There were no associated urinary or bowel symptoms.

Physical examination at that time revealed normal vital signs and moderate tenderness in the right lower quadrant of the abdomen associated with the suprapubic mass, supposedly the uterus. It was the opinion of the initial examiner that on pelvic examination the uterus was depressed into the pelvis, filling the posterior segment, and that it was tender on motion and slightly irregular in outline. The impression on admission was that the patient had an intrauterine pregnancy with a degenerating fibroid and she was transferred to the obstetrical ward.

Fig. 2.

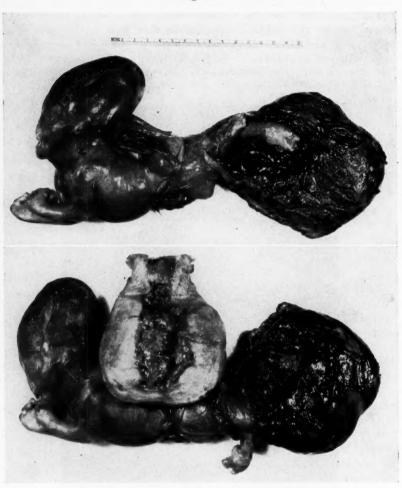


Fig. 3.

Figs. 2 and 3.—Photographs of gross specimens. Fig. 2 shows the relationship of the fetus and the placenta to the Fallopian tube. Fig. 3 pictures the uterus which has been opened along its anterior surface and its relative position to the fetus and placenta.

A second history taken on the admitting floor was essentially the same as that previously recorded except for the fact that the patient now related that she had felt no fetal movement although the calculated length of gestation was over twenty-one weeks. At repeat pelvic examinations after sedation the corpus uteri was poorly defined and to one examiner was angulated acutely into the cul-de-sac, tender on motion, and quite irregular in outline. The impression on admission was that of a questionable degenerating fibroid, a twisted ovarian cyst, and the remote possibility of a tuboovarian pregnancy.

On the day after admission a repeat pelvic examination was carried out, at which time it was noted again that the uterus was difficult to outline. In the cul-de-sac a large 8 by 15 cm. soft, nodular, tender mass was palpated, which could be moved slightly. The cervix was patulous and there was a brownish discharge emitting from the os. Rectal examination confirmed these findings. In addition some calcified areas were thought to be present. The diagnosis at that time was then changed to a dermoid cyst with some torsion, a missed abortion, and questionably some fibroids. An Aschheim-Zondek test was then ordered and a flat plate of the abdomen taken. The preliminary reading of the flat plate of the abdomen (Fig. 1) revealed the fetus of approximately twenty weeks' gestation; in addition there was a soft tissue mass in the lower pelvis which was thought originally to represent a distended bladder.

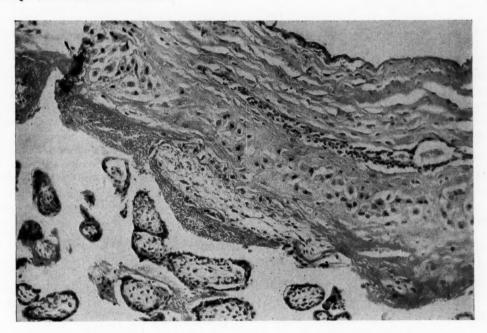


Fig. 4.—Photomicrograph of section taken through the maternal surface of the placenta. Note the villi and decidua and their relationship to the smooth muscle.

The patient was placed on bed rest and the vital signs were very closely observed. The abdominal pain increased in intensity and a laparotomy was advised and carried out on Sept. 5, 1953. Upon opening the peritoneal cavity a considerable amount of fresh and old clotted blood was encountered; this was estimated to be 1,000 c.c. Examination of the pelvic viscera showed the uterus to be approximately three times normal size. There were two masses, the largest of which was 24 by 6 by 5 cm., and within this mass there was a semisolid structure which had the configuration of a fetus. Attached was a globular mass of approximately 8 cm. in diameter, which later proved to be the placenta. The two masses were attached to the mesosalpinx on the right. The right ovary was found to be perfectly normal. The left tube and ovary had been removed. A right salpingectomy and a total hysterectomy were carried out. The patient received 1,000 c.c. of whole blood and seemed to tolerate the procedure well.

Her postoperative course was slightly febrile during the first three days with the temperature rising no higher than 101° F. Thereafter, the entire course was afebrile but was complicated by thrombophlebitis which was treated satisfactorily with bed rest, elevation of the lower extremities, and anticoagulation drugs for fifteen days. Examination on discharge revealed that the abdominal incision and the vaginal closure were well healed and the patient was discharged to be followed in the Sloane Follow-Up Clinic.

Pathological Examination .-

Macroscopic examination: The specimen consisted of a separate placenta, fetus, and fragmented saclike structure. The placenta measured 10.5 by 12 by 2.5 cm. The fetal surface was grossly normal, but was loosely covered with a thin, intact layer of translucent, light-red tissue. The maternal surface was covered by densely adherent tissue which was mottled yellow and red, and throughout which areas of increased opacity were seen. Attached to the maternal surface was the previously described saclike structure; this ras homogeneous, light pink in color, and superficial vessels were seen coursing through be external and internal surfaces. The feet and hips of the fetus protruded through a rent in this structure. The cord was dark, hemorrhagic, but otherwise normal, measuring 30 cm. in length. The fetus was male, badly macerated, weighed 320 grams, and measured 26 cm. in length (Figs. 2 and 3).

Also included was the uterus, which weighed 305 grams. The endometrial cavity was lined by a thick layer of light, whitish-tan succulent tissue. The myometrium was 4 cm. in thickness.

Microscopic Examination: Sections taken through the maternal aspect of the placenta revealed villi which were variable in size and shape. Most were shrunken and in only a few could vascular channels be demonstrated. In proximity to these villi was a badly fragmented structure throughout which hyperplastic smooth muscle fibers could be seen (Fig. 4). There were many large polygonal cells with pale cytoplasm and round central nuclei throughout. These were thought to represent decidual cells. Trophoblasts were not seen.

Sections through the junctions of sac and fetal surface of the placenta revealed fusion of amnion and chorion. The sac was lined by a thin fibrous structure adjacent to which was noted badly fragmented epithelium. Once again infrequent bundles of smooth

Microscopic examination of the tissue lining the endometrial cavity showed a typical decidual reaction.

### Reconstruction

It is felt that an intratubal gestation of approximately five and one-half months is satisfactorily demonstrated. Whether the pregnancy developed in an outpouching or a diverticulum of the tube, or in a tube which expanded generally with the growth of the pregnancy is not clear.

### Summary

In this case the diagnosis was not entirely unsuspected. The fairly classical history of previous ectopic gestation, sudden abdominal pain, and physical findings of a tender adnexal mass in the first trimester were strongly suggestive. The subsidence of symptoms and continuation of pregnancy until the second trimester were unusual. The historical succession of events which included lack of quickening, unusual pelvic findings, and an atypical flat plate of the abdomen prompted an exploratory celiotomy. The microscopic sections clarified the original site of placentation.

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## STRANGULATION OF PELVIC VARICOCELE IN PREGNANCY\*

## Case Report

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OCASIONAL cases of rupture of varicose veins in the broad ligament have been noted, but a search of the literature fails to reveal any case where an acute surgical abdominal crisis resulted from strangulation of a pelvic varicocele by compression between the anterolateral surface of the uterus and the abdominal wall. Such a case was encountered by us recently.

Curtis¹ has called attention to the marked distention of the veins in the uppermost portions of the broad ligaments which is occasionally seen late in pregnancy. As is pointed out by Eastman,² the blood from the ovary and upper part of the broad ligament is collected by a number of veins which form a large plexus within the broad ligament, the pampiniform plexus. These veins drain into the ovarian vein, which empties on the right into the vena cava and on the left into the left renal vein. Like varices of the legs, they may fail to involute following delivery, resulting in the persistence of a pampiniform plexus of varicose veins. This constitutes a varicocele in the mesosalpinx, analogous to the scrotal varicocele so common in males.

Davis<sup>3</sup> states that the condition is usually bilateral but is more pronounced on the left because of the indirect drainage of the left ovarian vein. The subinvoluted retroverted uterus containing fibroids and accompanied by relaxation of the pelvic floor with prolapse is the most frequent clinical syndrome associated with pelvic varicocele. The natural dextrorotation so often noted at the time of cesarean section was undoubtedly a predisposing factor in the following case, as it was present to a marked degree when the abdomen was opened.

### Case Report

M. H., a 34-year-old Caucasian, married, para iii, gravida iv, was admitted to the Kapiolani Maternity and Gynecological Hospital on Nov. 19, 1952, complaining of agonizing pain in the whole lower abdomen with marked tenderness in the left lower quadrant. This had begun as a gradual dull ache which had become unbearable. She was seen at her home by Dr. F. C. Carty and admitted at once to Kapiolani Hospital with the tentative diagnosis of ruptured uterus, probably involving the site of an old cesarean section scar. Fetal heart tones, heard at home, could no longer be heard after hospital admission. An alternate diagnosis was premature placental separation.

Her past history had mainly to do with pregnancies and was otherwise essentially negative. Her first pregnancy in 1935 ended with a normal term delivery of a 7½ pound infant, low forceps with the head on the perineum. This child died of a "brain tumor"

<sup>\*</sup>Read before the Staff Meeting of the Straub Clinic, June 22, 1953.

at 11 years of age. Her second delivery in 1938 was spontaneous, with the birth of an 8 pound child who survived. In 1947, with the third pregnancy, low cervical cesarean section was performed. After thirty-six hours of active labor with a persistent right occiput posterior, the cervix failed to dilate over 6 cm. in the presence of ruptured membranes and strong uterine contractions. The lower uterine segment was opened through a transverse crescentic incision (Munro-Kerr). Convalescence was uncomplicated.

Her last normal menstrual period occurred March 30, 1952. Estimated date of confinement was Jan. 6, 1953. About 10:00 A.M. on the date of admission, Nov. 19, 1952, the gradual onset of dull persistent pain was noted. This was most marked in the left lower quadrant of the abdomen although it involved the entire lower abdomen at first. Nausea and vomiting were absent. By late afternoon, the pain had become unbearable. At no time had there been noted any abnormal fetal activity and the patient did not remember having felt the fetus move since "some time before noon."

There was general agreement, on examination and consultation, as to the probable diagnosis and urgency of immediate surgery. Fetal heart tones could not be heard, but neither was auscultation satisfactory, due to the exquisite tenderness of the lower abdomen, most marked in the left lower quadrant just above Poupart's ligament.

Under 1 per cent Novocain local anesthesia with hyaluronidase, the abdomen was opened through the old subumbilical midline scar. On entering the peritoneal cavity, a mass of distended purple varicosities as large as a fist was immediately encountered. It was compressed between the left anterolateral surface of the uterus in its upper portion, and the peritoneal surface of the abdominal wall. No free blood or other fluid was seen. The uterus was noted to be in marked dextrorotation.

Fearing that embolism or rupture of the varicose mass might occur at the slightest touch, the abdominal incision was first lifted vertically upward at right angles to the long axis of the patient with a hooked finger at each end as a retractor. The operator now lifted the right side of the uterus by inserting a hand behind it so as to rotate the uterus slightly to the left around its long axis. The mass of veins then slipped back into the gutter to the left of the uterus and immediately collapsed until its bulk was reduced by at least one-half. All involved tissues appeared viable. It was identified as a pelvic varicoccle arising in the left pampiniform plexus. Veins were also prominent in the right broad ligament but to a lesser degree than on the left.

Having reduced the varicocele in size and replaced the mass of veins to approximately their anatomical position, we were now in a quandary. There still remained the possibility of some weakness of the uterine incision which seemed on inspection and palpation to be well healed. The consensus of the operator and his teammates was in favor of emptying the uterus, reasoning that the dextrorotation and accompanying strangulation of the varicocele might recur without this through persistence of pre-existing predisposing factors. Also, our inability to hear fetal heart tones made us consider the coexistence of an abruptio placentae.

Accordingly, the uterus was entered through the former incision site, a transverse crescentic incision in the lower segment. No weakness was noted, and no abruption was found. A large amount of meconium-stained amniotic fluid was evacuated. A living 5 pound, 4 ounce male fetus was then obtained, that was flaccid, cyanotic, and in generally poor condition. The features were those of a Mongoloid-idiot type. The infant died an hour after delivery by section. At autopsy, the heart showed a huge congenital interauricular defect. The mother's convalescence was uneventful, and she was discharged on the eighth postoperative day.

#### Comment

As a rule, standard obstetrical textbooks in dealing with varicose veins scarcely mention varicosities of the broad ligament. Most articles referring to varicoceles in the female seem to appear in the South American literature and are concerned with the occurrence of varicocele in the absence of preg-

nancy. A very occasional case of rupture of a varicosity of the broad ligament during pregnancy has been reported, and one such case was encountered by Dr. R. T. West, of this department. However, I have been unable to find a single case record of strangulation of broad ligament varicocele in pregnancy. So far as we can tell, the reported case is unique.

The differential diagnosis is among, chiefly, rupture of the uterus (especially if there has been a previous cesarean section), ruptured varix in the broad ligament, abruptio placentae with concealed hemorrhage, torsion of an ovarian cyst or pedunculated fibroid, and rupture of an ovarian cyst.

Etiological factors are: (1) subinvolution of the uterus and adjacent structures in multiparas; (2) anatomical arrangement of the left ovarian vein which empties directly into the left renal vein and predisposes to varicocele (the right ovarian vein has a longer course and empties into the vena cava); (3) dextrorotation in the pregnant uterus, bringing the left broad ligament forward toward the abdominal wall in a favorable location for being caught between the abdominal and anterior uterine walls in advanced pregnancy. It is a condition unlikely to be diagnosed before operation.

## Summary

- 1. Acute abdominal emergencies involving varicose veins of the broad ligament and occurring late in pregnancy are rare.
- 2. Occasional cases of ruptured pelvic varices are reported but so far as we know none have been noted of strangulation of a varicocele late in pregnancy prior to this case report.
  - 3. Differential diagnosis and etiological factors are discussed.
  - 4. Preoperative diagnosis is unlikely.

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## EXTRACTOR INSTEAD OF FORCEPS

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IT IS frequently necessary to consider means of shortening the second stage of labor in order to reduce the danger for the mother and for the child. For this purpose the obstetrical forceps are today used all over the world.

The principles of their use have been gradually developed over many years. Paul Portal, as early as 1685, expressed the opinion that the dilatation of the cervix should be left to natural processes. Later, Denman proposed that labor should be ended with the use of forceps whenever the second stage had lasted six hours and all other means of delivery had been tried. His pupil, Merriman (1810), however, extracted the child, whenever his life was threatened in the second stage of labor, after waiting two hours. Williams was also of the opinion that forceps should be used when the second stage lasted over two hours. More generally accepted today, however, is the rule (Siebold) that there is no time limit for the second stage, but that the endangered child or the mother may require the use of the forceps at any time.

Many users have tried to change the original shape of the forceps or in some way to improve the instrument. Hugh Chamberlain was among the first to employ such an instrument and claimed to know a safe way to end the delivery without danger for mother or child. Up to the present, the original shape of the forceps has been changed about two hundred times.

William Hunter (1718-1783) tells us that sometimes this instrument can be very dangerous and that it "brought the world more accidents than happiness." Georg Winter says that an enormous number of mothers and children were victims of the everyday use of the forceps and he calls it "a most dangerous instrument."

The fetal mortality from the use of forceps varies widely with the indications for which it is employed. Some authors, evidently referring to mid or high forceps, have reported figures as high as 12.4 per cent, whereas others have indicated a fetal death rate as low as 1 per cent. To the mortality must be added a variable morbidity, including injuries to bones, nerves, or skin as well as intracranial bleeding, which may show their consequences later in life.

Because of the great danger, the use of high forceps is today avoided. When necessary the child has been delivered by other means, even with the use of strings (Pierre Amand, André Levret) or, as has been tried in Japan, by means of a device employing sticks and silk ribbons (Seisu).

James Simpson (1851) also experimented with a special device for application to the child's head. In New York MacCahey tried to use his "air-tractor"

in emergency cases, but, lacking the knowledge of asepsis and anesthesia and as a result of some unexpected complications, nothing was accomplished from the use of such instruments.

#### Extractor

The "extractor" to be described in this article is a bell- or horn-shaped instrument the wider end of which is covered with rubber (Fig. 1). This end is inserted in the vagina and applied to the child's head. The other end is attached to a rubber tube, which permits the exhaustion of the air from the extractor by means of a syringe. When the necessary vacuum is achieved the tube may be closed by a stopcock. When applied in such a way to the child's head the extractor can be held firmly by the handles and pulled as desired, or a weight of about six pounds can be hung to it so that traction may be evenly and gradually applied until the child is delivered.



Fig. 1.—Extraction with a 200 c.c. syringe.

The instrument is very easy to insert in the multipara but in the primipara a small episiotomy under local anesthesia is advisable. The advantages of the extractor are many because it is a round-shaped instrument which can do harm neither to the mother's organs nor to whatever part of the child's body to which it is applied (Figs. 2 and 3).

#### **Maternal Indications**

The maternal indications for the use of the extractor during delivery in the second stage of labor are as follows: (1) weak labor pains and/or weak bearing down efforts; (2) moderate disproportion between the child and the soft parts of the genital tract, which may be easily overcome; (3) impending rupture of the uterus when there is no disproportion or obstacle to overcome during delivery from below; (4) premature separation of the placenta; (5) fever during delivery, of genital origin; (6) eclampsia and other types of severe toxemia; (7) general illness, such as diseases of heart, lungs, or kidneys, and other states which could be improved by delivery.

#### **Fetal Indications**

There is always an indication for the use of the extractor in childbirth when fetal life is in danger, as indicated by a fetal heartbeat of less than 100 per minute even though this increases in the intervals between labor pains,

or by a fast heart rate of above 160 a minute which does not decrease in the intervals between labor pains. There is danger also when the child's heart is beating irregularly or arrhythmically.



Fig. 2.—Extractor applied to child's head after delivery.



Fig. 3.—Suction power of extractor is demonstrated by lifting a child after delivery.

# Contraindications

Indications not to use the extractor are always present when it increases the danger for the mother or for the child: (1) cephalopelvic disproportion as a result of a large child or small pelvis; hydrocephalus and tumors of the child's head; abnormal position of the head, preventing the passage of the child through the genital canal; (2) tumors of the uterus, ovary, and other organs which are in the way and are obstructing the passage of the child's body; (3) abnormal position of the child, such as transverse presentation; (4) contraction of the birth canal which does not allow the correct application of the extractor; (5) unruptured membranes which should be perforated before the use of the extractor.

When the child is dead, the extractor is used only for sentimental reasons to avoid delivering the child piecemeal.

# Preparations for the Use of the Extractor

The patient is prepared in the usual way. The bladder and intestines are emptied, the hair is shaved, and the exterior of the genitals disinfected.

The special sterilized instruments that must be available include the extractor, a syringe of 200 to 300 c.c. capacity, and sutures in case of episiotomy. The patient's position is as during a normal delivery.

First, we must know the exact position of the child in relation to the genital canal. Anesthesia is not necessary except in special cases. Often we do give light anesthesia and we use a local anesthetic if episiotomy is necessary.

The extractor is inserted gently until the wider end rests on the child's head or any part of the body which presents. Now with a syringe we take the air from the instrument pumping it two or three times. When the desired vacuum is obtained we close the horn-shaped instrument with a little stopcock situated on the rubber tube. By palpation we can determine if the rubber-padded end rests properly on the child's head or body.

Now, simply by pulling by hand of by means of a weight of 3 kg. (about 6 pounds) we extract the child.

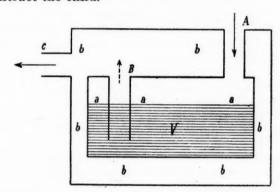


Fig. 4.—Explanation of extractor's action by a modification of Sellheim's drawing.

#### Extracting the Child With the Extractor

According to Sellheim's concept, a child is forced out during delivery by physiological forces, the contractions of the uterus and the pressure of the abdominal muscles. These forces are effective from above. Using the extractor, we add to the contraction power from above additional power on the opposite side from below.

We can compare this procedure with a hydraulic experiment explained in Fig. 4. The water can be forced out of the vessel in two ways, either by pressure on the upper surface or by suction from the bottom from under the water's surface. The result is the same whether we put pressure on the opening A or extract the air through the pipe C. In both cases the water comes out on the opening B.

We can compare the pressure through A to the labor contractions, and the extracting of the air through C as the pulling of the extractor.

#### Advantages of the Extractor Instead of Forceps

The advantages of the extractor over the conventional forceps may be listed as follows:

1. The extractor is a light, round-shaped instrument so it cannot injure the child or the mother's organs. It is not inserted deep into the genital tract and does not go over the child's head, so no harm can result to the mother's

genitals. Although parts of the child's body where the extractor is applied sometimes show a slight mark, this disappears shortly after delivery something like a caput succedaneum artificiale. Since the child's head is not pressed, there is no danger therefore to inner cranial parts.

2. The insertion is very simple and the extractor can for that reason be used by doctors who are not experts. It is possible to apply the extractor to any part of the child's body which is suitable to hold the vacuum and which is nearest to the exit.

3. During extraction the child can be turned in every way without danger. It is possible for the extraction to be made quickly by hand or slowly and evenly with the use of weights.

4. The extractor is lightly constructed, easy to carry, easy to prepare, and easy to clean.

#### Results

In the Obstetrical and Gynecological Department of the General Hospital at Rijeka there are delivered annually from 1,350 to 1,600 children. The incidence of cesarean section is a little over 2 per cent.

During the last three years, or since October, 1950, the use of forceps has been completely discontinued. The extractor has been used in 132 cases, 103 of these being deliveries of primiparas.

The weights of the children so delivered were as follows: less than 2,500 grams, 5; 2,500 to 4,000 grams, 109; over 4,000 grams, 21. The fetal indications included threatened asphyxia in 83 cases; large baby, 9 cases; prolapse of the cord, 1 case; prolapse of a hand, 2 cases. The maternal indications included uterine inertia, 91 cases; slightly contracted pelvis, 8 cases; eclampsia, 1 case; and myoma of the uterus, 1 case.

There were 3 instances of twins. The vertex was presenting in all but 5 cases, there being 1 brow and 4 breech presentations. Twice the extractor was used upon an already dead child.

There were no deaths or complications attributable to the extractor.

We can conclude that the extractor is in every way much simpler and easier to handle than forceps and is perfectly safe for mother and child.

## Summary

The extractor is an instrument shaped like a horn or like a bell which can be used in the second stage of labor to extract the child. This instrument is far less dangerous than forceps and much easier to handle. Instead of requiring deep insertion over the child's head or any part of his body, the extractor is simply applied to the part of the body nearest the operator. After applying the extractor and making a vacuum in the instrument, the extraction of the child becomes easy. It can be done quickly by hand or slowly and evenly with the help of traction and a weight of about 6 pounds.

In our department the extractor has been used successfully in 132 cases. There were no complications or accidents to mothers or delivered children.

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# AN INSTRUMENT FOR VAGINAL HYSTERECTOMY

R. C. CREELMAN, M.D., BREMERTON, WASH.

A SET of instruments has been devised which are felt to have a definite place in the technique of vaginal hysterectomy. For the accomplished surgeon who is performing the operation frequently and has his own particular technique well worked out, they are of far less value than to the neophyte mastering this difficult "inside-out, upside-down surgery." The orderliness which they make possible should appeal to any surgeon.

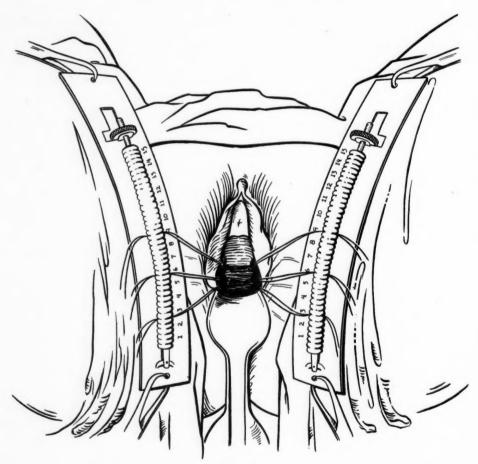


Fig. 1.

The tangle of instruments hanging over the perineum in a mass of blood clots is a common sight in most operating rooms. Uncertainty as to positive identification of some of the ligatures passing deeply into the vagina is doubtless a more common occurrence than many would admit.

The object of this set of instruments is to facilitate the holding and identifying of ligatures applied in surgical operations, especially vaginal hysterectomy, thereby reducing operating time and affording positive identification and reliable orientation throughout the operation.

These introital ligature holders and identifiers are comprised of two elongated strips of malleable metal conformable to either side of the vaginal introitus. These strips are secured in place by towel clips clamped to the skin or drapes through holes in either end. The coils of a helical spring with plural gripping elements mounted on the base strip serve as clamps for individual ligatures. Appropriate indicia marked on the base strip at different locations along its length afford a means of identifying the various ligatures pressed into the coils of the spring at such locations.

Adjustable means are provided for placing the spring initially under a certain amount of tension so as to create the desired pressure on the ligatures pressed between the coils. By virtue of this tension adjusting arrangement, the curvature of the base strip, hence of the spring, is permitted to be varied in conformity with the contour to which it is applied.

When the reconstruction of the supports of the vaginal vault is begun, the ligatures may be either disengaged from the coils of the spring by traction or cut free, as they are utilized.

# Department of Reviews and Abstracts

EDITED BY LOUIS M. HELLMAN, M.D., BROOKLYN, N. Y.

# Review of New Books\*

Progress in Clinical Surgery. A Symposium. Edited by Rodney Smith. 414 pages with 112 illustrations. Boston, 1954, Little, Brown & Co. \$7.50.

An analysis of recent advances in general and specialized surgical fields is presented in *Progress in Clinical Surgery*. It succeeds admirably in supplementing the standard surgical books and has maximal value for the postgraduate student or practicing surgeon. Twenty authors have surveyed general and limited surgical topics with emphasis on practical clinical considerations. The illustrations are adequate and the comprehensive references include many British and United States publications. The format of the book is pleasant and the descriptive language simple and clean.

An understanding of pathologic physiology and biochemistry in relation to surgical therapy is frequently stressed. These interrelationships are unusually well discussed in the chapters on "General Peritonitis" and "Fluid Replacement in the Surgical Patient" with occasional specific reference to gynecologic surgery.

There are thirty chapters which are thoroughly informative and present mainly general surgical subjects with some discussion of gynecologic and urologic entities.

Many common surgical illnesses have been deliberately omitted, presumably because of their excellent coverage in the standard texts. This book, therefore, is selective, supplementary, and intended for the physician who has already learned the fundamentals of clinical surgery.

I recommend the book highly for anyone engaged in general surgical or gynecologic practice.

Therapeutique Hormonale en Gynecologie et Obstetrique. By R. Vokaer. 278 pages with 59 illustrations. Paris, 1954, Masson & Cie. 2,200 fr.

This book chronicles the advances in hormonal physiology and therapy which have been made in the last twenty years as applied to gynecology and obstetrics. It is divided into three sections: the first dealing with menstruation; the second with the methods of investigation of the various endocrinological syndromes; and the third with the various hormonal agencies available for therapy.

Included in the first section is a discussion in great detail of the causation and the histiophysiologic mechanism of menstruation. Also in this section are listed all of the many examinations for the study of all major and minor gynecologic endocrinopathies, including the various chemical, metabolic, hormonal, and pathologic procedures which are available. Variations of the normal are mentioned and the range of abnormal findings in the different metabolic disturbances is demonstrated. The second section discusses fully the pathogenesis and treatment of amenorrhea, dysmenorrhea, and functional metromenorrhagia. A complete review of ovulation, sterility, and spontaneous abortion is also in-

<sup>\*</sup>The Advisory Committee on Policy has agreed that most book reviews need not be signed.

cluded in this section. The third section includes a rationale of hormonal therapy for all of the major symptom complexes associated with the sexual sphere. The value of estrogens, both natural and synthetic, of progesterone, of androgens, of the gonadotropins, of the cortico-adrenal and ACTH hormones, as well as of the thyroid, is presented in detail. The interrelationship of these endocrine secretions also is mentioned.

The author ably draws upon his own personal experiences as a researcher, teacher, and clinician. He has attempted to describe the actual conditions in gynecology and obstetrics where hormonal therapy is of value. Exact clinical syndromes are described, the basic hormonal pathology discussed, and the rationale of treatment explained. This is done in such a manner that the text can be used for reference not only by the general practitioner, but also by the gynecologist and endocrinologist as well.

In general the book is well constructed, clear and easy to read and digest. The contents are well documented and complete, and the illustrations well drawn or photographed.

Die biologischen Voraussetzungen einer Superfetation der Frau. By Ludwig Neuhaus. 67 pages with 11 illustrations and 5 tables. Stuttgart, 1954, Ferdinand Enke. D.M. 12.

The author explores exhaustively the factors in the vagina and cervix that foster or hinder the progress of spermatozoa from the portio vaginalis to the egg. The previous literature is reviewed at length and some new experimental data are supplied. Despite the title, the author discusses the migration of sperm in general, with particular emphasis on changes in the cervical mucosa and mucus during the menstrual cycle, and gives only incidental consideration to the changes that occur in pregnancy. He comes to the well-documented conclusion that the chief factor in the migration of sperm is the physical and chemical changes in the mucous plug and that this is most unfavorable to the sperm during pregnancy. Thus, superfetation is very unlikely even if ovulation occurs and the cornua are not occluded by decidua.

The subject matter is systematically and lucidly presented in a monograph which combines the previous knowledge in this field with valuable original work.

A Doctor Talks to Women. By Samuel Raynor Meaker. 231 pages. New York, 1954, Simon & Schuster, Inc. \$3.95.

The subtitle of this book, "What They Should Know About the Normal Functions and Common Disorders of the Female Organs," is an accurate and complete description of the contents of the volume. The author's huge experience in the field of gynecology is apparent. His easy manner of presentation and clarity without ridiculous simplicity make the volume especially noteworthy. The material presented is well organized and the information is generally accurate and reliable. A sincere effort is made to present the various attitudes toward diagnoses and treatment in those fields where there is recognized difference of opinion.

The first chapter is concerned with the anatomy of the genitourinary system of the female. Subsequent chapters include such titles as "The Functions of the Ovaries," "Normal Menstruation," "The Change of Life," "Abnormal Bleeding," "Painful Menstruation," "Fertility and Sterility," "Ways in Which Early Pregnancy May Go Wrong," "Cancer," "Operations," "X-Rays and Radium," "Douches," "Treatment With Hormones," and a very commendable chapter entitled "The Mind Can Influence the Body."

The appendix, consisting of "definitions of medical terms," is very well done. This will give any person who reads this book an adequate vocabulary to discuss with her physician or other laymen the anatomy and physiology of the female genitourinary tract. Also, the volume is well indexed.

The author is to be congratulated on having presented a great deal of information in a concise and easily understandable manner.

Surgical Treatment of Cancer of the Cervix. By Joe V. Meigs. 462 pages. New York, 1954, Grune & Stratton, Inc. \$12.00.

The current revival of interest in the surgical approach to carcinoma of the cervix has been under the aegis of Dr. Joe V. Meigs. It is only fitting that his contribution to gynecology be memorialized in a splendid volume under his editorship. He has approached this task with great humility and forthrightness. Through such an approach, we may learn the real role of surgery in this condition.

For the presentation of the anatomy of the pelvis and the significance of lymph nodes and lymph channels of the pelvis, Dr. Meigs has called on Drs. William Quinby, Erle Henriksen, and Carl Javert. This aspect of the surgical treatment is very well defined and portrayed by these authors. The functional disturbances of the pelvic viscera following radical surgery are discussed in a chapter devoted to the sympathetic and parasympathetic nerves of the ureters and bladder.

The reader will find the techniques of radical hysterectomy with bilateral dissection of the pelvic lymph nodes not only thoroughly discussed but beautifully illustrated in a section composed by Drs. Bayard Carter, Joe Meigs, Paul Werner, and Julius Sederl. Many of the pitfalls that beset both the expert and the neophyte are lucidly presented. It is apparent that there is still no uniformity of opinion on what constitutes an adequate radical hysterectomy. In addition, Drs. Werner and Sederl add to the discord with the statement: "Lymph nodes and their surrounding areolar and fatty tissues are removed only if the nodes are enlarged."

Other surgical approaches, such as the radical vaginal hysterectomy, the partial and complete pelvic exenterations, and the retroperitoneal lymph node dissection, are described in considerable detail by men of vast experience in this field. A succinct but adequate section is devoted to the ureters and bladder in radical pelvic surgery.

Although the various surgical procedures so well presented in this volume do not permit one to draw any statistical conclusions as to the comparative merits of radiation and surgery, Dr. Meigs is to be commended for his straightforward and excellent compilation of current thoughts and techniques in the surgical treatment of cancer of the cervix. This book should be read and studied by all who contemplate the treatment of patients with cancer of the cervix—whether the choice be radiation or surgery. The two methods of treatment should be partners and not rivals in the attack on the disease.

Legal Medicine, Pathology and Toxicology. By Thomas A. Gonzales, Morgan Vance, Milton Helpern, and Charles J. Umberger. 1349 pages. New York, 1954, Appleton-Century-Crofts, Inc. \$22.00.

Although this tome contains a vast amount of information that is highly technical and specialized, the average reader will be fascinated by the authors' presentation of the various aspects of legal medicine. The criminal and legal problems associated with pregnancy, rape, and sterility are amply discussed. It behooves all practicing obstetricians and gynecologists to acquaint themselves with the forensic entanglements associated with these conditions.

In a chapter entitled, "The Rights and Obligations of Physicians: Malpractice," the authors delve into such topics as criminal and civil malpractice, torts, privileged communications, dying declarations, and hospital liabilities. In this age of legal suits, the physician should be familiar with the significance of this phase of medicine, and thereby avoid the pitfalls that beset many an unwary individual.

This reviewer agrees with the statement of Harrison Martland in the introduction that "this book so completely and thoroughly covers the subject of legal medicine and toxicology that it should become the handbook and daily guide for the coroner, the

coroner's physician, the county physician, the medical examiner, the toxicologist and the pathologist." In addition, the obstetrician and gynecologist will find it a valuable reference for the reasons stated earlier in this review.

Atlas of Human Anatomy. By Franz Frohse, Max Brödel, and Leon Schlossberg. 88 pages with 71 illustrations. New York, 1954, Barnes & Noble, Inc. \$2.00.

This pocket-sized volume is a very poor entry into a field of many valuable publications. It is unfortunate that the original Frohse-Brödel wall charts, which were so beautiful and clear, have lost their qualities in miniature reproduction. The explanatory text is poorly composed and certainly not designed for either medical students or physicians.

Sandoz' Atlas of Haematology. 91 pages with 255 illustrations. Basle, Switzerland, 1952, Sandoz, Ltd. \$7.00.

In my opinion this is by far the best atlas of hematology. The illustrations are all photomicrographs, beautifully reproduced as to color and cellular detail. There is an unusually complete set of illustrations of all the cell types and diseases, including several pictures of carcinoma cells in the marrow, and even adventitious elements such as sebaceous gland cells.

The accompanying text is brief and to the point. This has been in constant use since it first came out in the French and German editions.

The Diagnosis and Treatment of the Infertile Female. By Fred A. Simmons. 83 pages with 6 illustrations. Springfield, Ill., 1954, Charles C Thomas. \$2.50.

The monograph is an outline of the procedures utilized in the management of the infertile marriage. The brevity of the book is unfortunate because the author's wide experience could have enabled him to report on several phases of the subject in greater detail. Many important topics are discussed in chapters of only two or three pages in length. In all fairness it may be said that the task of compressing the entire subject adequately into such a small volume is insurmountable. The book, therefore, limits its attractiveness to those who are interested in a rapid review of some of the diagnostic and therapeutic aids in the care of the infertile woman.

Reproductive System. By Frank H. Netter. 286 pages. Summit, N. J., 1954, Ciba. \$13.00.

Any atlas correlating anatomy and surgical pathology is destined to receive some adverse comment from the purist. Some may criticize from an anatomic view that omissions of detail have been made which are sine qua non. The artist may complain that the drawings lack realism. There are pathologists who may feel that the illustrations do not depict the true form or color of the diseased tissues. Dr. Netter and his collaborators realized that these objections would arise and stated as much in the introduction. All the plates, however, are compilations and are presented in a semischematic form. Details were excluded when it was felt that they were superfluous or confusing to a more important fact.

The scope is extensive, covering such aspects of the male and female reproductive systems as embryology and development, anatomy, endocrinology, disease, trauma, diagnosis, and even the surgical management of some of these entities. This publication may be best appreciated if considered as a basic reference rather than an all-inclusive treatise on any of these topics. The anatomical plates attempt to combine the systemic and regional approach. The author selected a most authoritative group of advisers and the text, therefore, is accurate and up to date.

Certain shortcomings are quite obvious. The small type selected for the descriptions and explanations makes reading often difficult. Microscopic views are oversimplified. The

color and tones of the plates are excessively red. If photomicrographs had been used for this feature, it would have made this important addition worth while. The bibliography is very scant.

Am. J. Obst. & Gynec. May, 1955

This volume is not destined to become one of the classical atlases for, in literature at least, quantity is no substitute for quality. It will, however, realize a substantial popularity for two reasons: first, it is timely for the practitioner and student in need of a textbook of this nature; second, it is relatively inexpensive since it is subsidized by private industry, and sold without profit.

Toxaemias of Pregnancy. John Sophian. 231 pages with 37 illustrations. London, 1953, Butterworth & Co., Ltd. 25s.

The theme of this book is that toxemia of pregnancy is the result of renal-cortical shutdown—the Trueta shunt. Franklin and Sophian noted blanching of the surface of the left kidney in the rabbit, when the uterus was distended by saline, blood, or other fluids. Amoroso-Centeno placed ligatures around the pregnant rabbit uterus, between fetuses. As the fetuses grew, the uterine wall became tense and a reflex diversion of the renal cortical flow ensued. These observations suggested that tension in the uterine wall (and to a lesser extent in the bladder and bowel walls) initiates a uterorenal reflex. This results in the Trueta shunting of the renal cortical blood flow to the renal medulla.

The author then ranges far and wide to pick out facts and fancies which can be incorporated into chains of reasoning to support this theme. The text abounds in such terms as "irrefutable evidence," "absolutely confirmed," "unchallengeable," "only possible conclusion," etc. A typical chain: sodium and water retention is perhaps fundamental in toxemia. Current hypotheses as to how the kidney handles salt and water are inadequate to explain all of the facts. The medulla makes up half of the kidney and must have some important function. Let us, then, look to the medulla for an explanation. The Trueta shunt would give the medulla dominance over the cortex. Therefore the abnormal salt and water retention of toxemia can be explained by the Trueta shunt. Reduced cortical blood flow might result in the release of several substances causing hypertension and at the same time cause proteinuria.

Many of the observations on eclampsia are brought into line with the thesis, for instance, the increased incidence of eclampsia in cold weather. Women in a delicate condition are reluctant to expose themselves to any chill. Therefore they allow their bladders and bowels to become distended. This reflexly initiates the Trueta shunt, and there you are with toxemia.

In a review of reasonable length, one can neither summarize Sophian's arguments adequately or fairly, nor criticize them in detail. The Trueta shunt may occur in rabbits, but there is no good evidence that it is operative in the human kidney. If it does exist, it is much more easily induced in the rabbit and one wonders why toxemia of pregnancy is not a rabbit disease rather than a human disease.

# Selected Abstracts\*

# Journal of Obstetrics and Gynaecology of India

Vol. 14, No. 9, September, 1953.

Chakravarti, J.: Incidence of Non-malignant Cervical Lesions in Gynaecological Practise and Their Influence on Fertility, p. 1.

Bhagat, Anusuya: Retained Placenta, p. 7.

Mitra, Subodh: Extended Radical Vaginal Hysterectomy for Cancer of the Cervix, p. 15.

Mitra, Subodh: Radiosensitivity of Epidermoid Carcinoma of the Cervix, p. 27.

Basu, Swadesh, Bhose, Lokenath, Choudhuri, R. Dutt, Basu, B., and Mitra, Subodh, Dir.: A Preliminary Report on the Estimation of Chorionic Gonadotrophin in Toxemia of Pregnancy, p. 30.

Choudhuri, Parijat, Mitra, Subodh, Choudhuri, R. Datta, and Basu, B.: Study on Pregnanediol Excretion in Toxemia of Pregnancy, p. 34.

Mitra, Sukumar, Sahay, P. A. S., Upadhyay, S. N., and Achari, G.: Comparative Study of Tetraethyl Ammonium Bromide and Hexamethonium Tests in Toxemias of Late Pregnancy, p. 41.

Ghose, D., et al.: Urge Incontinence Syndrome in Women, p. 46.

Krishman, P. B.: A Clinical Review of 400 Cases of Prolapse of the Uterus, p. 53.

Phatak, Leela V.: A Study of Abdominal Measurements in One Thousand Women at Term, p. 62.

Mitra, K. N., et al.: Analysis of the Results of Treatment of Antepartum Hemorrhage at the Eden Hospital From February to July, 1952, p. 68.

Devi, N. Subhadra: Sacculation of the Uterus With Report of a Case, p. 75.

Ghose, D., et al.: Hydatiform Mole in Fallopian Tube, p. 81.

Mitra, K. N., et al.: On the Role of Teaching Hospitals as Key Maternity Centres in India, p. 85.

Vol. 14, No. 12, December, 1953.

\*Kreibich, Harald Dr. med.: Conservative Therapy of Genital Diseases With Consideration of Inoperable Cases, p. 303.

Kreibich: Conservative Therapy of Genital Diseases With Consideration of Inoperable Cases, p. 303.

An old technique using a new drug, Dondren, is described for prolapse of the uterus in the advanced age groups where surgery is contraindicated from a medical standpoint. Dondren is a mineral oil nearly insoluble in alcohol, which is used by injection into the parametria under sterile conditions. This insoluble foreign element produces a sterile inflammation with proliferation of connective tissue resulting in a lipogranuloma. Clinically this reaction causes a "scirrhous shrimping in the area of injection," ultimately causing retraction of the pelvic organs into the vagina. The method of injecting an insoluble substance to create a foreign-body granulomatous reaction was first described by Halban in 1900.

<sup>\*</sup>Titles preceded by an asterisk are abstracted below.

Thirty-six cases are reported with an 80 to 85 per cent cure rate during a nine-month follow-up. The technique of injection is simply described. The author feels the drug should be used only in inoperable cases because, in failures with this technique, it is very difficult to do an adequate plastic operation.

JOSEPH J. SMITH, M.D.

Vol. 15, No. 1, January, 1954.

Rominger, E.: Vitamin Deficiency and Vitamin Therapy in Infancy and Childhood, p. 1.

Vol. 15, No. 2, February, 1954.

30th All-India Medical Conference, p. 31.

The Use of Dondren in Gynaecology-Abstract, p. 51.

Vol. 15, No. 3, March, 1954.

Achaya, S.: The Cervix Uteri, p. 65.

Jain, S. P.: Anatomy of the Cervix Uteri, p. 77.

Reynolds, S. R. M.: A Physiologist Examines the Cervix, p. 93.

Wahi, P. N.: Vaginal Cytology in Early Detection of Cervical Cancer, p. 102.

Singh, Manmohan, and Singh, Gurbachan: Pathology of Cervix, p. 109.

Runge, H., and Back, H. G.: Simple Ulcer of the Cervix, p. 116.

Schubert, Gerhard: Fundamentals in Diagnosis and the Treatment of Carcinoma in Situ of Cervix, p. 123.

Vol. 15, No. 4, April, 1954.

Mayer, A.: Carcinoma of Cervix and Pregnancy, p. 145.

Vol. 15, No. 5, May, 1954.

Wepsi, H. J.: Colposcopy in the Diagnosis of Cervical Pathology, p. 171.

# Anais brasileiros de ginecologia

Vol. 36, No. 4, October, 1953.

\*Mello, Vought, and Portella: The Prevention of Congenital Syphilis, p. 193.

\*Araujo, and Guariento: Considerations About Brow Presentation, p. 203.

Article on the Obituary of Dr. Thomas Stephen Cullen (1869-1953), p. 221.

Mello, Vought, and Portella: Prevention of Congenital Syphilis, p. 193.

The authors point out that syphilis in many countries is becoming a rare disease. The great improvement in methods of attack by public health authorities and their wholesale application throughout the United States during the last two decades have been most important contributions. The prenatal law of 1938, its provisions and importance are discussed.

JOHN PARENTE, M.D.

#### Araujo and Guariento: Brow Presentation, p. 203.

This is a report of 11 cases of brow presentation which occurred in 10,027 deliveries. In this series persistent brow presentation occurred once in 911 cases. There were no maternal deaths, and the corrected fetal mortality was 9 per cent. Cesarean section was performed in 54.5 per cent of cases, and 27.2 per cent were delivered by forceps. The authors advocate the early evaluation of cephalopelvic disproportion, emphasizing that cesarean section is less dangerous to the fetus, in cases of borderline or contracted pelvis, than extraction by forceps after the cervix is fully dilated and the presenting part well engaged.

JOHN PARENTE, M.D.

Vol. 36, No. 5, November, 1953.

- \*Limburg, Hans: Histological Findings in Cancer of the Body of the Uterus, p. 249.
- \*Fernandes, Alves, and Neto: Rupture of the Uterus, p. 259.
- \*Grabois and Schneider: The Role of Psychology in Gynecology, p. 267.

# Limburg: Histological Findings in Cancer of the Body of the Uterus, p. 249.

In a histological review on 363 cancers of the uterus from the Gynecological Clinic of the University of Hamburg between 1920 and 1951 it was possible to study the endometrium, particularly in extirpated uteri.

- In 7 per cent secretory endometrium and carcinoma were found simultaneously.
- In 10 per cent, proliferative endometrium and carcinoma.
- In 50 per cent, cystic glandular hyperplasia and carcinoma.
- In 10 per cent, regression hyperplasia and carcinoma.
- In 23 per cent, atrophic endometrium and carcinoma.

Therefore a carcinoma of the uterus may be found simultaneously with any type of endometrium, hyperplasia being predominant. It is conceded that follicular hormone may enhance action of the actual carcinogenic factors on the cells. Warning is directed toward misuse of the follicular hormone at the menopause.

JOHN PARENTE, M.D.

# Fernandes, Alves, and Neto: Rupture of Uterus, p. 259.

The incidence of rupture of the uterus at the Encruzilhada Maternity Hospital is 1 in 351 cases. In two-thirds of such cases, however, the uterus had already ruptured when the patient came to the clinic; one-third ruptured at the clinic. Of these 18 patients, in 13 there was no apparent cause for the accident, in 5 it followed a major obstetric procedure, in 3 cases version and in 2 cases extraction.

JOHN PARENTE, M.D.

#### Grabois and Schneider: Role of Psychology in Gynecology, p. 267.

The authors criticize as well as offer suggestions regarding the role played by psychology in gynecology and the so-called psychosomatic disturbances.

A critical psychoanalysis relative to the problem of femininity is touched upon. The attributes considered as the basis of the characterization of female personality are correlated, in accordance with the degree of culture.

JOHN PARENTE, M.D.

#### Vol. 36, No. 6, December, 1953.

- \*de Moraes, Arnaldo: Carcinoma of the Cervix, "Stage O." p. 313.
- \*Linhares: Total Urinary Neutral 17-Ketosteroids Assay, p. 323.
- A Report on the First World Congress of Fertility and Sterility, p. 335.

# de Moraes: Carcinoma of Cervix, "Stage O," p. 313.

This was the official Report to the Convention of Brazilian Gynecologists in November, 1952. The definition is stated as resolved by "The International and Fourth American Congress on Obstetrics and Gynecology" in New York, in May, 1950. Conclusions reached are that a great deal of misunderstanding and contradiction regarding Stage O cervical carcinoma still exist. The hope of better understanding lies in detection and follow-up clinics.

JOHN PARENTE, M.D.

#### Linhares: Total Urinary Neutral 17-Ketosteroids Assay, p. 323.

The purpose of the article was the study of the adrenocortical metabolism during pregnancy, by 17-ketosteroid determinations.

Various methods of assay are discussed.

In normal pregnancies the results were within the normal range; in 2 cases of patients treated with cortisone, high titers were found.

JOHN PARENTE, M.D.

Vol. 37, No. 1, January, 1954.

\*Queiroz, Boto, and Maia: Total Hysterectomy in Nonmalignant Conditions of the Uterus, p. 1.

Queiroz, Boto, and Maia: Total Hysterectomy in Nonmalignant Conditions of the Uterus, p. 1.

The authors support the opinion that total hysterectomy instead of subtotal should be performed in nonmalignant conditions of the uterus. After supravaginal hysterectomy, 50 per cent of the patients complained of symptoms connected with lesions of the cervical stump. Histopathological studies of 67 uteri extirpated by total hysterectomies disclosed 3 clinically unsuspected cases of carcinoma (4.47 per cent).

JOHN PARENTE, M.D.

Vol. 37, No. 2, February, 1954.

\*Queiroz, Batinga: Aureomycin and Iodochloroxyquinoleine in the Treatment of Trichomonas Vaginitis, p. 65.

\*Bezerra, Pedroza: Saddle Block Anesthesia in Obstetrics, p. 75.

Queiroz: Aureomycin and Iodochloroxyquinoleine in the Treatment of Trichomonas Colpitis, p. 65.

Among 25 patients treated with Aureomycin locally (500 mg. with talcum) 2 have developed intolerance (8 per cent); 17 were cured (68 per cent); 4 failures (16 per cent); and 2 developed Monilia infection (8 per cent).

A series of 25 patients were treated with a combination of iodochloroxyquinoleine and formo-cibazol, with Fenocyclin additional; after 90 days of active treatment, 84 per cent were cured and in 16 per cent the treatment failed.

JOHN PARENTE, M.D.

Bezerra: Saddle Block Anesthesia in Obstetrics, p. 75.

After summarizing the history of spinal anesthesia in obstetrics, the authors describe the technique. They use the Parmley method, slightly modified.

JOHN PARENTE, M.D.

# Revista colombiana de obstetricia y ginecologia

Vol. 5, No. 3, December-January, 1953-1954.

A Discussion on the Application of Mid- and High Forceps, p. 129.

Bastidas: Chorionepithelioma, p. 135.

Ofman, José: Comments on a Case of Fibromyoma Associated With Pregnancy, p. 147.

#### Bulletin of the New York Academy of Medicine

Vol. 30, No. 9, September, 1954.

\*Vogel, Peter: Current Problems in Blood Transfusion, p. 657.

Vogel: Current Problems in Blood Transfusion, p. 657.

This timely and authoritative article reviews the problems and methods of the proper collection and administration of blood and substitutes at a time when these products are being used in ever-increasing amounts. In a period of less than four years, over 42,000

blood transfusions have been administered at the Mount Sinai Hospital, New York City.

The donor must be carefully examined to prevent the transmission of various diseases, particularly syphilis, malaria, and viral hepatitis. *Treponema pallidum* is destroyed if blood is kept at refrigerator temperature for ninety-six hours. No such protection is afforded against Plasmodium. Contrary to popular belief, irradiation does not preclude the risk of transmission of viral hepatitis.

Newer methods for the preservation of blood for prolonged periods of time are outlined. The necessity for newer techniques in this field is illustrated by the fact that, following storage of blood with standard preservatives, about 30 per cent of the transfused cells do not survive more than twenty-four hours in the recipient.

The direct matching by the indirect antiglobulin test is strongly urged as the method of choice whenever a patient has had previous blood transfusions to detect isoimmunization produced by the recently discovered minor antibodies, i.e., Rh, Hr, K, Fya, M, S, s, Jka, and Fyb.

The intravenous route is preferred for the rapid administration of blood. The advantages of intra-arterial transfusion have not been proved and it carries with it the danger of producing gangrene of the involved limb.

The author is not encouraged by the use of the so-called "blood substitutes"—albumin, modified protein such as polyvinylpyrrolidone (PVP), and dextran. They do not effectively combat hemorrhagic shock and they are responsible for a high percentage of allergic reactions.

The increased use of blood therapy has led to a corresponding increase in the number of transfusion reactions. Incompatibility of the main blood groups is responsible for the more severe reactions. The administration of 300 c.c. of improperly matched blood usually produces a critical condition. Pyrogens are the most common cause of reactions but these are usually mild. Allergic reactions may frequently be prevented by the simultaneous administration of an antihistamine substance.

Exogenous hemochromatosis is nowadays a more frequently encountered complication in cases which require repeated transfusions because the body lacks a mechanism for the elimination of the excess iron.

GERALD S. STOBER, M.D.

Vol. 30, No. 10, October, 1954.

Berson, Solomon A.: Blood Volume in Health and Disease, p. 750.

#### Journal of the American Geriatrics Society

Vol. 2, No. 11, November, 1954.

Lane, W. H., Jr.: A New Boon to the Aged—Relief of Nocturnal Leg Cramps, p. 736. Heckel, N. J.: Diagnosis and Treatment of Diseases of the Bladder in the Aged, p. 746.

# Items

# American Board of Obstetrics and Gynecology

Applications for certification (American Board of Obstetrics and Gynecology) for the 1955 Part I Examinations are now being accepted. Candidates are urged to make such application at the earliest date possible. Deadline date for receipt of applications is Oct. 1, 1955.

All candidates for admission to the examinations are required to submit with their application a plain typewritten list of all patients admitted to the hospitals where they practice, for the year preceding their application or the year prior to their request for reopening of their application, with the diagnosis, pathological diagnosis, nature of treatment, and end result.

Applications for re-examination, as well as requests for resubmission of case abstracts, must also be made to the Secretary prior to Oct. 1, 1955. Such requests must be made in the form of a letter and not by telephone.

Current Bulletins may be obtained by writing to the Secretary's office.

ROBERT L. FAULKNER, M.D., Secretary 2105 Adelbert Road Cleveland 6, Ohio

## First Venezuelan Congress on Obstetrics and Gynecology

The First Venezuelan Congress on Obstetrics and Gynecology was held in Caracas, Jan. 11 to 16, 1955. Over three hundred doctors from sixteen countries attended. Papers were read in Spanish, Portuguese, and English, and translations were made during the presentations. Dr. P. Gutierrez Alfaro, Minister of Health, was the honorary president. Dr. J. Calcano was president, and Dr. R. Pittaluga C. was secretary.